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(54) Title: GENE EXPRESSION PROFILES IN NORMAL AND CANCER CELLS

(57) Abstract

As a step towards understanding the complex differences between normal and cancer cells, gene expression patterns were examined in gastrointestinal tumors. More than 300,000 transcripts derived from at least 45,000 different genes were analyzed. Although extensive similarity was noted between the expression profiles, more than 500 transcripts that were expressed at significantly different levels in normal and neoplastic cells were identified. These data provide insights into the extent of expression differences underlying malignancy and reveal cancer that are verified as disconsists or prospection was transcripted. genes that are useful as diagnostic or prognostic markers.

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Gene Expression Profiles in Normal and Cancer Cells

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TECHNICAL FIELD OF THE INVENTION

This invention is related to the diagnosis of cancer, and tools for carrying out such diagnosis.

BACKGROUND OF THE INVENTION

Much of cancer research over the past 50 years has been devoted to the analyses of genes that are expressed differently in tumor cells compared to their normal counterparts. Although hundreds of studies have pointed out differences in the expression of one or a few genes, no comprehensive study of gene expression in the cancer cell has been reported. It is therefore not known how many genes are expressed differentially in tumor versus normal cells, whether the bulk of these differences are cell autonomous rather than being dependent on the tumor microenvironment, and whether most differences are cell-type specific or tumor specific. Thus there is a need in the art for information on the molecular changes that occur in cells during cancer development and progression.

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SUMMARY OF THE INVENTION

According to one embodiment of the invention, a method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

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comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

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identifying the first sample as neoplastic when the level of the at least one transcript is found to be lower in the first sample than in the second sample.

According to another embodiment of the invention, another method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

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comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

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identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

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In another embodiment of the invention an isolated and purified human nucleic acid molecule is provided. The molecule comprises a SAGE tag selected from SEQ ID NO:1-732.

In yet another aspect of the invention an isolated nucleotide probe is provided. The probe comprises at least 12 nucleotides of a human nucleic acid molecule, wherein the human nucleic acid molecule comprises a SAGE tag selected from SEQ ID NO: 1-732.

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According to another aspect of the invention a method is provided for diagnosing pancreatic cancer in a sample suspected of being neoplastic. The method comprises the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

According to still another embodiment of the invention a method of diagnosing cancer in a sample suspected of being neoplastic is provided. The method comprises the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

According to another embodiment of the invention a method is provided to aid in the determination of a prognosis for a colon cancer patient. The method comprises the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

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determining a poorer prognosis if the level of the at least one transcript is found to be lower in the first sample than in the second sample.

According to another aspect of the invention a method to aid in determining a prognosis for a patient with colon cancer is provided. The method comprises the steps of:

comparing the level of at least one transcript in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

In yet another embodiment of the invention a method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of expression of the protein is found to be lower in the first sample than in the second sample.

In another aspect of the invention a method of diagnosing colon cancer in a sample suspected of being neoplastic is provided. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript

identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

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According to another embodiment of the invention a method is provided to aid in determining a prognosis of a patient having pancreatic cancer. The method comprises the steps of:

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comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

determining a poorer prognosis if transcription is found to be higher in the first sample than in the second sample.

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In yet another aspect of the invention a method to aid in providing a prognosis for a cancer patient is provided. The method comprises the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

determining a poorer prognosis if transcription is found to be higher in the first sample than in the second sample.

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According to still another aspect of the invention, a method is provided for diagnosing pancreatic cancer in a sample suspected of being neoplastic. The method comprises the steps of:

comparing the level of expression of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

According to yet another aspect of the invention a method is provided for diagnosing cancer in a sample suspected of being neoplastic. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

In still another embodiment of the invention a method is provided to aid in the determination of a prognosis of a colon cancer patient. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of expression is found to be lower in the first sample than in the second sample.

In still another embodiment of the invention a method is provided to aid in determining a prognosis for a patient with colon cancer. The method comprises the steps of:

comparing the level of expression of at least one protein in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and

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wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

In still another aspect of the invention a method is provided to aid in determining a prognosis of a patient having pancreatic cancer. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

According to even a further aspect of the invention a method is provided to aid in providing a prognosis for a cancer patient. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

In still another embodiment of the invention a method of treating a cancer cell is provided. The method comprises the step of:

administering to a cancer cell an antibody which specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5, wherein the antibody is linked to a cytotoxic agent.

In another aspect of the invention an antibody linked to a cytotoxic agent is provided. The antibody specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5.

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According to another aspect of the invention, a method of detecting colon cancer in a patient is provided. The method comprises the steps of:

comparing the level of at least one protein or transcript in a first

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body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of

blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

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In another aspect of the invention a method of detecting pancreatic cancer in a patient is provided. The method comprises the steps of:

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comparing the level of at least one protein or transcript encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Also provided by the present invention is a method of detecting cancer in a patient. The method comprises the steps of:

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comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Additionally provided by the present invention is a method to aid in the determination of a prognosis for a colon cancer patient. The method comprises the steps of:

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comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a colon cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 3, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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determining a poorer prognosis if the level of the at least one protein or transcript is found to be lower in the first sample than in the second sample.

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Provided by another embodiment of the invention is a method to aid in determining a prognosis for a patient with colon cancer. The method comprises the steps of:

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comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

According to still another aspect of the invention, a method to aid in determining a prognosis of a patient having pancreatic cancer is provided. The method comprises the steps of:

comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Also provided by the present invention is a method to aid in providing a prognosis for a cancer patient. The method comprises the steps of:

comparing the level of expression of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

The present invention further includes antisense oligonucleotides complementary in whole or in part to SEQ ID NOS:1-732.

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This invention also provides a method for screening for candidate agents that modulate the expression of a polynuleotide selected from the group consisting of the polynucleotides in SEQ ID NOS.1-732 or their respective complements, by contacting a test agent with a pancreatic or colon cell and monitoring expression of the polynucleotide, wherein the test agent which modifies the expression of the polynucleotide is a candidate agent.

The present invention provides the art with new methods and reagents for diagnosing and prognosing cancers. In addition, some of the newly disclosed genes may play an important role in the development of cancers.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1. Comparison of expression patterns in colorectal cancers and normal colon epithelium. (FIG. 1A) A semi-logarithmic plot reveals 51 tags that were decreased more than 10 fold in primary CR cancer cells whereas 32 tags were increased more than 10 fold. 62,168 and 60,878 tags derived from normal colon epithelium and primary CR cancers, respectively, were used for this analysis. The relative expression of each transcript was determined by dividing the number of tags observed in tumor and normal tissue as indicated. To avoid division by 0, a tag value of 1 was used for any tag that was not detectable in one of the samples. These ratios were then rounded to the nearest integer and their distribution plotted on the abscissa. The number of genes displaying each ratio was plotted on the ordinate. Tu: CR tumors; NC: Normal colon. (FIG. 1B and FIG. 1C) Differentially expressed genes in The number of transcripts found to be differentially colorectal cancers. expressed (P < 0.01) are presented as Venn diagrams. Diagrams of transcripts that were decreased (FIG. 1B) or increased (FIG. 1C) in CR cancers compared to normal colon epithelium. Comparisons were between primary tumors and cells in culture as indicated.

Fig. 2. Northern blot analysis of genes differentially expressed in gastrointestinal neoplasia. Northern blot analysis was performed on total RNA (5 μg isolated from primary CR carcinomas (T) and matching normal colon epithelium (N), or pancreatic carcinomas. The top panel in each case show an

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example of the ethidium bromide stained gels prior to transfer. The number of SAGE tags observed in the original analysis is indicated to the right of each blot. (FIG. 2A) Examples of transcripts that were decreased or increased in CR cancers. (FIG.2B) Examples of transcripts increased in pancreatic cancers (10). (FIG.2C) Examples of transcripts elevated in cancer which were or were not cancer type specific. Probes used for Northern blot analysis were as follows (Human SAGE Tag unique identifier, gene name, (GenBank accession number)): (FIG. 2A) H204104, Guanylin (M95714); H259108, (see Table 2); H1000193, (see Table 2); H998030, (see Table 2). (FIG. 2B) H294155, RIG-E (U42376); H560056, TIMP-1 (S68252). (FIG. 2C) H802810, EST338411 (W52120); H85882, 1-8D (X57351); H618841, GA733-1 (X13425).

Tables 2-5. Transcripts Differentially Expressed in Human Cancer.

Tag sequence represents the NlaIII site plus the adjacent 11 bp SAGE tag. Tag number indicates a SAGE UID (unique identifier). NC, TU, CL, PT, PC, refers to the number of the indicated tag observed in RNA isolated from normal colorectal epithelium, primary colorectal cancers, colorectal cancer cell lines, primary pancreatic cancers, or pancreatic cancer cell lines, respectively. The Accession and Gene Name refer to representative GenBank entries that contain the tag sequence.

Table 2 Transcripts increased in colorectal cancer.

Table 3 Transcripts decreased in colorectal cancer.

Table 4 Transcripts increased in pancreatic cancer.

Table 5 Transcripts increased in pancreatic and colorectal cancer.

DETAILED DESCRIPTION

The inventors have discovered sets of human genes which are either upregulated or downregulated in cancer cells, as compared to normal cells. Specifically, certain genes have been found to be upregulated or downregulated in colorectal and/or pancreatic cancer cells, when compared to normal colon

cells. These sets of differentially regulated genes can be used as diagnostic markers, either individually or in sets of, for example, 2, 5, 10, 20, or 30.

Genes whose expression was detected to be increased in colorectal cancer are shown in Table 2. Genes whose expression was detected to be decreased in colorectal cancer are shown in Table 3. Genes whose expression was detected as increased in pancreatic cancer are shown in Table 4. Genes whose expression was detected as increased in both pancreatic cancer and colorectal cancer are shown in Table 5. These latter genes likely play a role in neoplastic development generally.

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Tag sequences, as provided herein, uniquely identify genes. This is due to their length, and their specific location (3') in a gene from which they are drawn. The full length genes can be identified by matching the tag to a gene data base member, or by using the tag sequences as probes to physically isolate previously unidentified genes from cDNA libraries. The methods by which genes are isolated from libraries using DNA probes are well known in the art. See, for example, Veculescu et al., Science 270: 484 (1995), and Sambrook et al. (1989), MOLECULAR CLONING: A LABORATORY MANUAL, 2nd ed. (Cold Spring Harbor Press, Cold Spring Harbor, New York). Once a gene or transcript has been identified, either by matching to a data base entry, or by physically hybridizing to a cDNA molecule, the position of the hybridizing or matching region in the transcript can be determined. If the tag sequence is not in the 3' end, immediately adjacent to the restriction enzyme used to generate the SAGE tags, then a spurious match may have been made. Confirmation of the identity of a SAGE tag can be made by comparing transcription levels of the tag to that of the identified gene in certain cell types.

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In addition to the sequences shown in SEQ ID NOS: 1-732, or their complements, this invention also provides the anti-sense polynucleotide stand, e.g. antisense RNA to these sequences or their complements. One can obtain an antisense RNA using the sequences provided in SEQ ID NOS: 1-732 and the methodology described in Vander Krol et al. (1988) BioTechniques 6:958.

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The invention also encompasses polynucleotides which differ from that of the polynucleotides described above, but which produce the same phenotypic effect, such as the allele. These altered, but phenotypically equivalent polynucleotides are referred to "equivalent nucleic acids." This invention also encompasses polynucleotides characterized by changes in non-coding regions that do not alter the phenotype of the polypeptide produced therefrom when compared to the polynucleotide herein. This invention further encompasses polynucleotides, which hybridize to the polynucleotides of the subject invention under conditions of moderate or high stringency.

The polynucleotides can be conjugated to a detectable marker, e.g., an enzymatic label or a radioisotope for detection of nucleic acid and/or expression of the gene in a cell. A wide variety of appropriate detectable markers are known in the art, including fluorescent, radioactive, enzymatic or other ligands, such as avidin/biotin, which are capable of giving a detectable signal. In preferred embodiments, one will likely desire to employ a fluorescent label or an enzyme tag, such as urease, alkaline phosphatase or peroxidase, instead of radioactive or other environmental undesirable reagents. In the case of enzyme tags, colorimetric indicator substrates are known which can be employed to provide a means visible to the human eye or spectrophotometrically, to identify specific hybridization with complementary nucleic acid-containing samples. Briefly, this invention further provides a method for detecting a single-stranded polynucleotide identified by SEQ ID NOS.1-732 or its complement, by contacting target single-stranded polynucleotides with a labeled, single-stranded polynucleotide (a probe) which is at least 10 nucleotides of the complement of SEQ ID NOS: 1-732 (or the corresponding complement) under conditions permitting hybridization (preferably moderately stringent hybridization conditions) of complementary single-stranded polynucleotides, or more preferably, under highly stringent hybridization conditions. Hybridized polynucleotide pairs are separated from un-hybridized, single-stranded polynucleotides. The hybridized polynucleotide pairs are detected using methods well known to those of skill in the art and set forth, for example, in Sambrook et al. (1989) supra.

The polynucleotides of this invention can be isolated using the technique described in the experimental section or replicated using PCR. The PCR technology is the subject matter of United States Patent Nos.4,683,195, 4,800,159, 4,754,065, and 4,683,202 and described in PCR: The Polymerase Chain Reaction (Mullis et al. eds, Birkhauser Press, Boston (1994)) or MacPherson et al. (1991) and (1994), supra, and references cited therein. Alternatively, one of skill in the art can use the sequences provided herein and a commercial DNA synthesizer to replicate the DNA. Accordingly, this invention also provides a process for obtaining the polynucleotides of this invention by providing the linear sequence of the polynucleotide, nucleotides, appropriate primer molecules, chemicals such as enzymes and instructions for their replication and chemically replicating or linking the nucleotides in the proper orientation to obtain the polynucleotides. In a separate embodiment, these polynucleotides are further isolated. Still further, one of skill in the art can insert the polynucleotide into a suitable replication vector and insert the vector into a suitable host cell (procaryotic or eucaryotic) for replication and amplification. The DNA so amplified can be isolated from the cell by methods well known to those of skill in the art. A process for obtaining polynucleotides by this method is further provided herein as well as the polynucleotides so obtained.

RNA can be obtained by first inserting a DNA polynucleotide into a suitable host cell. The DNA can be inserted by any appropriate method, e.g., by the use of an appropriate gene delivery vector or by electroporation. When the cell replicates and the DNA is transcribed into RNA; the RNA can then be isolated using methods well known to those of skill in the art, for example, as set forth in Sambrook et al. (1989) supra. For instance, mRNA can be isolated using various lytic enzymes or chemical solutions according to the procedures set forth in Sambrook et al. (1989), supra or extracted by nucleic-acid-binding resins following the accompanying instructions provided by manufactures.

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Polynucleotides having at least 10 nucleotides and exhibiting sequence complementarity or homology to SEQ ID NOS: 1-732 find utility as hybridization probes. In some aspects, the full coding sequence of the transcript, i.e., for SEQ ID NOS: 1-732, are known. Accordingly, any portion of the known sequences available in GenBank, or homologous sequences, can be used in the methods of this invention.

It is known in the art that a "perfectly matched" probe is not needed for a specific hybridization. Minor changes in probe sequence achieved by substitution, deletion or insertion of a small number of bases do not affect the hybridization specificity. In general, as much as 20% base-pair mismatch (when optimally aligned) can be tolerated. Preferably, a probe useful for detecting the aforementioned mRNA is at least about 80% identical to the homologous region of comparable size contained in the previously identified sequences identified by SEQ ID NOS:1-732, which correspond to previously characterized genes or SEQ ID NOS:1-732, which correspond to known ESTs. More preferably, the probe is 85% identical to the corresponding gene sequence after alignment of the homologous region; even more preferably, it exhibits 90% identity.

These probes can be used in radioassays (e.g. Southern and Northern blot analysis) to detect, prognose, diagnose or monitor various pancreatic or colon cells or tissue containing these cells. The probes also can be attached to a solid support or an array such as a chip for use in high throughput screening assays for the detection of expression of the gene corresponding to one or more polynucleotide(s) of this invention. Accordingly, this invention also provides at least one of the transcripts identified as SEQ ID NOS:1-732, or its complement, attached to a solid support for use in high throughput screens.

The total size of fragment, as well as the size of the complementary stretches, will depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the complementary region may be varied,

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such as between about 10 and about 100 nucleotides, or even full length according to the complementary sequences one wishes to detect.

Nucleotide probes having complementary sequences over stretches greater than 10 nucleotides in length are generally preferred, so as to increase stability and selectivity of the hybrid, and thereby improving the specificity of particular hybrid molecules obtained. More preferably, one can design polynucleotides having gene-complementary stretches of more than 50 nucleotides in length, or even longer where desired. Such fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, by application of nucleic acid reproduction technology, such as the PCR technology with two priming oligonucleotides as described in U.S. Pat. No. 4,603,102 or by introducing selected sequences into recombinant vectors for recombinant production. A preferred probe is about 50-75 or more preferably, 50-100, nucleotides in length.

The polynucleotides of the present invention can serve as primers for the detection of genes or gene transcripts that are expressed in pancreatic or colon cells. In this context, amplification means any method employing a primer-dependent polymerase capable of replicating a target sequence with reasonable fidelity. Amplification may be carried out by natural or recombinant DNA-polymerases such as T7 DNA polymerase, Klenow fragment of E.coli DNA polymerase, and reverse transcriptase.

A preferred amplification method is PCR. However, PCR conditions used for each reaction are empirically determined. A number of parameters influence the success of a reaction. Among them are annealing temperature and time, extension time, Mg²⁺ ATP concentration, pH, and the relative concentration of primers, templates, and deoxyribonucleotides. After amplification, the resulting DNA fragments can be detected by agarose gel electrophoresis followed by visualization with ethidium bromide staining and ultraviolet illumination.

The invention further provides the isolated polynucleotide operatively linked to a promoter of RNA transcription, as well as other regulatory

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sequences for replication and/or transient or stable expression of the DNA or RNA. As used herein, the term "operatively linked" means positioned in such a manner that the promoter will direct transcription of RNA off the DNA molecule. Examples of such promoters are SP6, T4 and T7. In certain embodiments, cell-specific promoters are used for cell-specific expression of the inserted polynucleotide. Vectors which contain a promoter or a promoter/enhancer, with termination codons and selectable marker sequences, as well as a cloning site into which an inserted piece of DNA can be operatively linked to that promoter are well known in the art and commercially available. For general methodology and cloning strategies, see Gene Expression Technology (Goeddel ed., Academic Press, Inc. (1991)) and references cited therein and Vectors: Essential Data Series (Gacesa and Ramji, eds., John Wiley & Sons, N.Y. (1994)), which contains maps, functional properties, commercial suppliers and a reference to GenEMBL accession numbers for various suitable vectors. Preferable, these vectors are capable of transcribing RNA in vitro or in vivo.

Fragment of the sequences shown in SEQ ID NOS:1-732 or their respective complements also are encompassed by this invention, preferably at least 10 nucleotides and more preferably having at least 18 nucleotides. Larger polynucleotides, e.g., cDNA or genomic DNA, which hybridize under moderate or stringent conditions to the polynucleotide sequences shown in SEQ ID NOS:1-732, or their respective complements, also are encompassed by this invention.

In one embodiment, these fragments are polynucleotides that encode polypeptides or proteins having diagnostic and therapeutic utilities as described herein as well as probes to identify transcripts of the protein which may or may not be present. These nucleic acid fragments can by prepared, for example, by restriction enzyme digestion of the polynucleotide of SEQ ID NOS:1-732, or their complements, and then labeled with a detectable marker. Alternatively, random fragments can be generated using nick translation of the molecule. For

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methodology for the preparation and labeling of such fragments, see Sambrook et al., (1989) supra.

Expression vectors containing these nucleic acids are useful to obtain host vector systems to produce proteins and polypeptides. It is implied that these expression vectors must be replicable in the host organisms either as episomes or as an integral part of the chromosomal DNA. Suitable expression vectors include viral vectors, including adenoviruses, adeno-associated viruses, retroviruses, cosmids, etc. Adenoviral vectors are particularly useful for introducing genes into tissues in vivo because of their high levels of expression and efficient transformation of cells both in vitro and in vivo. When a nucleic acid is inserted into a suitable host cell, e.g., a procaryotic or a eucaryotic cell and the host cell replicates, the protein can be recombinantly produced. Suitable host cells will depend on the vector and can include mammalian cells, animal cells, human cells, simian cells, insect cells, yeast cells, and bacterial cells constructed using well known methods. See Sambrook et al. (1989) supra. In addition to the use of viral vector for insertion of exogenous nucleic acid into cells, the nucleic acid can be inserted into the host cell by methods well known in the art such as transformation for bacterial cells; transfection using calcium phosphate precipitation for mammalian cells; or DEAE-dextran; electroporation; or microinjection. See Sambrook et al. (1989) supra for this methodology. Thus, this invention also provides a host cell, e.g. a mammalian cell, an animal cell (rat or mouse), a human cell, or a procaryotic cell such as a bacterial cell, containing a polynucleotide encoding a protein or polypeptide or antibody.

When the vectors are used for gene therapy in vivo or ex vivo, a pharmaceutically acceptable vector is preferred, such as a replication-incompetent retroviral or adenoviral vector. Pharmaceutically acceptable vectors containing the nucleic acids of this invention can be further modified for transient or stable expression of the inserted polynucleotide. As used herein, the term "pharmaceutically acceptable vector" includes, but is not limited to, a vector or delivery vehicle having the ability to selectively target

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and introduce the nucleic acid into dividing cells. An example of such a vector is a "replication-incompetent" vector defined by its inability to produce viral proteins, precluding spread of the vector in the infected host cell. An example of a replication-incompetent retroviral vector is LNL6 (Miller, A.D. et al. (1989) BioTechniques 7:980-990). The methodology of using replication-incompetent retroviruses for retroviral-mediated gene transfer of gene markers is well established (Correll et al. (1989) PNAS USA 86:8912; Bordignon (1989) PNAS USA 86:8912-52; Culver, K. (1991) PNAS USA 88:3155; and Rill, D.R. (1991) Blood 79(10):2694-700. Clinical investigations have shown that there are few or no adverse effects associated with the viral vectors, see Anderson (1992) Science 256:808-13.

Compositions containing the polynucleotides of this invention, in isolated form or contained within a vector or host cell are further provided herein. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

This invention further encompasses genes, either genomic or cDNA, which code for a polypeptide or protein in the cell of interest. The genes specifically hybridize under moderate or stringent conditions to a polynucleotide identified by SEQ ID NOS: 1-732 or their respective complements. The process of identification of larger fragment or the full-length coding sequence to which the partial sequence depicted in SEQ ID NOS:1-732 hybridizes preferably involves the use of the methods and reagents provided in this invention, either singularly or in combination.

Five methods are disclosed herein which allows one of skill in the art to isolate the gene or cDNA corresponding to the transcripts of the invention.

RACE-PCR Technique

One method to isolate the gene or cDNA which code for a polypeptide or protein and which corresponds to a transcript of this invention, involves the 5'-RACE-PCR technique. In this technique, the poly-A mRNA that contains the coding sequence of particular interest is first identified by hybridization to

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a sequence disclosed herein and then reverse transcribed with a 3'-primer comprising the sequence disclosed herein. The newly synthesized cDNA strand is then tagged with an anchor primer of a known sequence, which preferably contains a convenient cloning restriction site attached at the 5'end. The tagged cDNA is then amplified with the 3'-primer (or a nested primer sharing sequence homology to the internal sequences of the coding region) and the 5'-anchor primer. The amplification may be conducted under conditions of various levels of stringency to optimize the amplification specificity. 5'-RACE-PCR can be readily performed using commercial kits (available from, e.g., BRL Life Technologies Inc, Clotech) according to the manufacturer's instructions.

Identification of known genes or ESTs

In addition, databases exist that reduce the complexity of ESTs by assembling contiguous EST sequences into tentative genes. For example, TIGR has assembled human ESTs into a datable called THC for tentative human consensus sequences. The THC database allows for a more definitive assignment compared to ESTs alone. Software programs exist (give examples) that allow for assembling ESTs into contiguous sequences from any organism.

Isolation of cDNAs from a library by probing with the SAGE transcript or tag

Alternatively, mRNA from a sample preparation was used to construct cDNA library in the ZAP Express vector following the procedure described in Velculescu et al. (1997) Science 270:484. The ZAP Express cDNA synthesis kit (Stratagene) was used accordingly to the manufacturer's protocol. Plates containing 250 to 2000 plaques are hybridized as described in Rupert et al. (1988) Mol. Cell. Bio. 8:3104 to oligonucleotide probes with the same conditions previously described for standard probes except that the hybridization temperature is reduced to room temperature. Washes are performed in 6X standard-saline-citrate 0.1% SDS for 30 minutes at room temperature. The probes are labeled with 32P-ATP through use of T4 polynucletoide kinase.

Table 2 - Transcripts increased in colon cancer

Transcripts increased in only colon primary tumors compared to normal colon (61 genes)

NC: Normal Colon

TU: Calon Primary Tumor CL: Culon Cancer Cell Line pT: Pancreatic Primary Tumor pC. Pancreatic Cancer Cell Line

ne	(1-t-[2] from	II (COIII) pse		, , ,			ene, partial cds	1).	shage colony-stimu	plete cds.	omniete cds	DMA complete	IIVIAN, compilere	Noith A Homo sap	AbilpA Homo sap	138925 5'.	attachment se	1486 similar to Mi	nifar to Human mi	eta (HLA-DR B).	PHKG2 homol		insactivator.	ZNF157 (ZNF15	sequence from HMC	omplete cds.	NFLS Homo sa	VFLS Homo sa
Gene Name	11 misochondrial BST sequence (1-t-12) from	H. Sapiens minocaconal in COIII) pse	Turnali cytochionic condens	H, sapiens mKIVA (Icial Dialil Colors Carry)	H.sapiens HNF1-C mRNA.	H.sapiens HNF1-B mRNA.	Human mitochondrion cytochrome b gene, partial cds	H.sapiens mRNA for transacylase (DBT)	Human mRNA for granulocyte-macrophage colony-stimu	Human thymonoietin beta mRNA, complete cds.	VNQ.	Human Inymopoletin gaminia mixi vy, compression	Human metastasis suppressor (R.A.11) IIINIAA, Complete	2b91h11.s1 Soares parathyroid tumor Nb14PA Homo sap	zc05d03.s1 Soares parathyroid tumor Nbl/IPA Homo sap	vil 1407,r1 Homo sapiens cDNA clone 138925 51.	H.sapiens mitochondrial DNA for loop attachment se	A 1486F Homo sapiens cDNA clone A 1486 slinilar to Mi	In 1870 Home capient cDNA 3'end similar to Human mi	District Annual Annual Property (HLA-DR B)	Human minima for the contraction of the contraction	phosphorylase Kinase cutalytic anomist	H. sapiens mRNA for MHC class II transactivator.	Human zinc finger containing protein ZNF137 (ZNF13	Human Iciomyoma LM-196.4 ectopic sequence from HMO	Human Fc alpha receptor b mRNA, complete cds.	za62h11,ri Soares fetal liver spleen INFLS Homo sa	za63f10.rl Soares fetal liver spleen INFLS Homo sa
Againfan	T	T		Z70701	X71347			X66785	Т	T	T	000088	U20770	W15552	W32091	Γ	Τ	T				S73483	X74301	U28687			Γ	W03770
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	NC	612	452	433	3		202	227	392					27	à			32	23	26	93		124				15	
	Tag Number	H285759	H933704	05100011	1200120		0000	H291282	H753750					310000	H681913			H130369	H965434	H175872	H177115		000300111	H1025522				HZ14010
	Tow Sequence	TO A TO A OCT A A TTGG	CALCACITATION OF THE	CAIGIGALLICACIL	CATGCCTGTAATCCC			CATGCACTACTCACC	S CATGGTGAAACCCCA(G)						6 CATGGGCTTTAGGGA			7 CATGACITTCCAAA	CATCTCCTCTATCCA		y CA GAGGGIOTO	IN CATCAGGICAGGAGAGA		II CATGTTGGCCAGGCT				12 CATGATCACGCCCTC

							W04748	za42109.r1 Soares fetal liver spleen INFLS Homo sa
13 CATGGGGGTCAGGGG	169669H	37	130		9	6	T12078 W45641	A730R Homo sapiens CDNA clone A730 sitting to mice 226a12.s1 Soares senescent fibrobiasts NbHSF Homo
_	01541780	ă,	4	2	25	12	D51017	Human fetal brain cDNA 3'-end GEN-007C04.
14 CATGGCTAGGTTTAI	1041100						D53694	Human fetal brain cDNA 3-end GEN-11/EU1.
	H350996	26	132	35	0	<u></u>		Unknown
	H183018	81	155	7	12	7	D\$102I	Human fetal brain clork 3 - and Cert-507 255
16 CATUAUTAGGGG					1	1	D51052	Human retail praint chive 3 - end GEN-089E01.
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JULIO 4 TOTOCOTTO	H388278	79	124	19	7	23	D83195	Human DINA (or Deuxyllboniaceae) Process
17 CATGCCTGTAGTCCC	H136465	64	121	28	77	2	D54113	Human icial main Control of the Control of 102-25) from
IS CATCACACCACACAC	H327364	49	107	35	7	8 -	F15796	H.Sapiens (Hitocalonalia) Ed. 200
19 CATGCATTION	H874182	28	78	4		<u>=</u>	10.000	It conjugated and DNA penomic Misel fragment, cl
20 CATOCCA ACCTCCT	H606582	23	22	∞		2	239183	Harman family brain cDNA 5'-end GEN-091D11.
17	,				1	1	D32503	11 colors mitorhardrial FST sequence (129-09) from
TUUUUTVUUUT	H609624	29	73	-	7	9	F16449	The supperson major and the configuration of the co
77 CA100000100001	H1027370	35	22	<u>~</u>	35	4	000432	Unitial Distance of the Control of t
23 CATGLIGGICAGG	1081801	07	49	11	15	26		231. 21 J GEN 006D02
24 CATGTCCTATIAAG	SCHOOL	2	47	7	-	4	D51004	Human fetal brain CDNA 3 - the CENT-0000 25.
25 CATGTTACTTATACI	0201260						1.49057	Homo sapiens retinal tovea ESI in In Do 10304 sequence:
		4				-	D\$1071	Human fetal brain cDNA 3'-end GEN-010E01.
	2500001	12	45	-	4	2		
26 CATGATGGCAGGAGT	CC/967H	2 0	1	,	~	3		1. 7 1 1
27 CATGCTAAGGCGAGG	H401411	7		۲	15	2	103592	Human ADP/ATP translocase mRNA, 3' end, clone prin 1
28 CATGGGTGAGACACT	H713234	-\	1	1	2 2	3	X57352	Human 1-8U gene from interferon-inducible gene fam
29 CATGACCTGTATCCC	H97078	اِم	44		3 -	3 0	H01571	vi33e06.rl Homo sapiens cDNA clone 150562 5' simil
30 CATGCCAGTCCGCCT	H339302	1	ŝ	>	-	,	H03072	yj46g12.rl Homo sapiens cDNA clone 151846 5' simil
		-	2.7	6	-	0	725155	EST730 Homo sapiens cDNA clone 34C11.
31 CATGTAATTTTIGCC	H802810	-	200	,		~	D50972	Human fetal brain cDNA 3'-end GEN-004A05.
T	H993Z64		5	*	1		D\$1211	Human fetal brain cDNA 3'-end GEN-017E08.
		1					D52162	Human fetal brain cDNA 3'-end GEN-0691'04.
		+					723865	seq2012 Homo sapiens cDNA clone Coll 3/4rt-4rb3/v/2-5
	2020000	-	3.5	-	9	0	M32053	Human H19 RNA gene, complete cds.
33 CATGGCCACCCCTG	H001/10)[<u>=</u>	1/2	61	33	15	X67247	H.sapiens rpS8 gene for ribosomal protein 36.
34 CATGTAATAAAGGTG	H/36/101	===	3 15	8	-	14	T11939	A953F Homo sapiens cDNA clone A953 similar to mito
35 CATGTACTGCTCGGA	11011021							

yeq2f01.s1 Homo sapiens cDNA clone 120409 3' simil 2335609.r1 Soares fetal liver spleen INFLS Homo sa		1 1 1			448 zb96h01.s1 Soares parathyroid tumor NbHPA Homo sap 782 zc40b06.r1 Soures senescent fibrobinsts NbHSF Homo		W31782 zb96a06.r1 Soares parathyroid tumor Northy Hours 3at M24398 Human parathymosin mRNA, complete cds.	U33317 Human defensin 6 (HD-6) gene, complete cds.		TI1701 A1225F Homo sapiens cDNA clone A1225 similar to MI		П	M10029 Figures appear Consequence of Policy Simila H11641 yml7e04.s1 Homo sapiens cDNA clone 199288 3' simil R95667 yq51a09.s1 Homo sapiens cDNA clone 199288 3' simil	M74090 Human TB2 gene mRNA, 3' end.
T95857 W03237	X54195 X54195 U29607	D29062 D29563	763196 Z57093 Z60184	W31349	W31448 W47282	X71428 S62140		EED .	M98331		1	-		
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36 CATGGTGAAACCCA	37 CATGGAAACTGAACA	38 CATGACTITITAAAA 39 CATGGACTGCGTGCC	40 CATGTCAGTGGTAGT 41 CATGAAACTGTGGTT		42 CATGGGGGGGGGGGGT 43 CATGGTGCCCGTGCC		i	45 CATGTCCTGCCCA1	47 CATGGGTATTAACCA	48 CATGGGCTACACCTI	49 CATGAGGGTGTTTCC 50 CATGCAAGGACCAGC		51 CATGTGGAAATGACC 52 CATGATCCGCCTGCC	53 CATGICCCGTACAC 54 CATGATGTAAAAAT

M19045 Human lysozyme mRNA, complete cas.	- 1	- 1					- 1			1	1	
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Transcripts increased in both colon primary tumors and colon cancer cell lines compared to normal colon (47 genes)

NC: Normal Colon

TU: Colon Primary Tumor CL: Colon Cancer Cell Line PT: Pancreatic Primary Tumor PC: Pancreatic Cancer Cell Line

Gena Name	Human ribosomal protein 1.28 mRNA, complete cds.	Human mRNA for LLNeps.	SCI MKNA	H. sapiens mRNA for 23 KD nignly dasic process	H.sapiens mRNA for etongation tactor 2.	H. sapiens S19 ribosomal protein mixty, compress of	Human acidic ribosomal phosphoprotein r.z. mich.	H sapiens hing mRNA for uracii DNA giycosymae.	Human glyceraldehyde 3-phospnare denydrogenase men	H.sapiens mRNA for clongation tactor-1-gamma.	Human pancreatic tumor-related protein mixiva, 3 cii	H.sapiens mRNA for ribosomal protein L3.	H. sapiens mRNA for ribosomal protein L3.	Himan novel gene mRNA, complete cds.	Human Wilm's furnor-related protein (QM) mRNA, comp	Jaminin receptor homolog (3' region) [human, mRNA	DIA Con OBE	Hisapiens miking to over	Human mKNA for noosonial protection mRNA c	Human ribosomal protein 34 (no 34/8) issues:	Human scar protein market, complete cast	H.saplens mRNA for neosonila protein 210.	Homo sapiens 18S ribosomat protein (many)	Human mRNA for T-cell cyclopanian.	Human DNA for insulin-like grown lactor 11 (101 2)	Human Bak mRNA, complete cas.	
Accession	П	$\overline{}$	X64707 H.sapiens BBCI mKNA	X56932 H.sapiens m	Z11692 H.sapiens m		M17887 Human acid	X53778 H.sapiens ht	J02642 Human glyc	Z11531 H.sapiens m	M55409 Human pand	Γ	T_	1	T	T	T	٦	╗	MS8458 Human ribx	\neg	X69150 H.saplens n	L06432 Homo sapic	Y00052 Human mR	X07868 Human DN		description of the second
Dd	138	294	250	147	190	134	73 185 MI	183		45 152 ZI		196 72	200	3	100 ly	MA	4	113 215 X8	122 XI	50 92 M	X	55 250 X		46 143 Y	0	50	-
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-	ng Number NC	\dagger	\dagger	\dagger	\dagger	\dagger	\dagger	\dagger	1801/40	13	1959498	+	H55227 30	H660601 36	H174037 47			1144683 48	\dagger	77	十	Ch 50222011	Hydodoo 42	86 0700000	+	\dagger	H482584 12
PC: Pancicault Canto	F	+		-	-	5 CATGAGCACCTCCAG	6 CATGCTGGGTTAATA	-	8 CATGTACCATCAATA	-	9 CATGTGGCCAAAGCC		IN CATGAATCCTGTGGA		CATO A GOO CITICO A A	-		1	+	+	15 CATGTCAGATCITIG		16 CATGTGGTGTTGAGG	+	\dashv	18 CATGCTTGGGTTTTG	19 CATGCTCCTCACCTG

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D14530 [Human homolog of yeast ribosomal protein S28, comp	X73974 H.sapiens HRPL4 mRNA.	٦	T	٦	X63527 H.sapiens mRNA for ribosomal protein L19.		U14967 Human ribosomal protein L21 mRNA, complete cds.	X55954 Human mRNA for HL23 ribosomal protein nomologue.	X52839 Human mRNA for ribosomal protein L17.		H71935 ys15f12.rl Homo sapiens cDNA clone 214693 3	Z43914 H. sapiens partial cDNA sequence; clone c-10003.	T48545 hbc3221 Homo sapiens cDNA clone incesza: 3 can.	X04347 Human liver mRNA fragment DNA binging protein Ora	X00910 Human mRNA for IGP-11 precursor (insuling graw	X61156 [H.sapiens mRNA for laminin-binding protein.	Π		Γ	T		L16785 Homo sapiens c-myc transcription factor (put) mRNA	L10376 Human (clone CTQ-B33) mRNA sequence.		M77349 Human transforming growth factor-beta induced gene	X58536 Human mRNA for HLA class I locus C heavy chain.	Г	Π		1	Π	Γ	W46476 324128 3.	X72718 H. sapiens DNA for orphan TCR V-beta segment (anex	
103		119	118	99	146	L	19	120	1	64				40	0	57		95	2 2	388		-	3		8	18	2	22	25	-	,	-	9		İ
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cell lines compared to normal colon (181 genes) Transcripts increased in only colon cancer

NC: Normal Colon
TU: Colon Primary Tumor
CL: Colon Cancer Cell Line
PT: Pancreatic Primary Tumor
PC: Pancreatic Cancer Cell Line

Seas Name		Human mRNA for clongation factor 1-eipina	Human ribosomal protein S12.	Himan cylokeratin 18.	(MPS1)	Homo sapiens metallopalishing (vir. 2.)	H sapiens B1 mRNA for mucin.	H. sapiens FRGAMMA mRNA (819bp) for folder receptor	1		Human folate receptor 3 mRNA, complete cas.		Ven2m2 r1 Homo supiens cDNA clone 116571 5.		T	T	Fluman illymosili octa 10	H.sapiens mRNA for ribosomal protein L31.	Human ribosomal protein 1.27a	H.sapiens ribosomal protein L11.	Τ	Т	Т	Т	Т	П	Т	7	Human ferritin L chain	
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Human elongation factor 1 delta (EF 1delta)	Human ribosomal protein S17 mKNA	Human triosephosphate isomerase	human alpha-tubulin	Homo sapiens ribosomal protein L27 (RPL27)	H.sapiens Ubago mRNA for ubiquitin.	Unknown	H.saplens ribosomal protein L6.	ym14a02.r1 Homo sapiens cDNA clone 47866 5'	ya31g04.r5 Homo sapiens cDNA clone 62262 5	yd98a05.r1 Homo sapiens cDNA clone 116240 5'	yi99c06.r1 Homo sapiens cDNA clone 147370 5	yw54e05.rI Homo saplens cDNA clone 230004 3.	ya75b09,rl Homo sapiens cDNA clone o (461 J.	yb55a12.rl Homo sapiens cDNA clone 75U/U 5.	Human heat shock protein hsp86.	Human ubiquitin carrier protein (E2-EPF)	H.sapiens transcription factor BTF 3.	Human beta-tubulin	H.sapiens mRNA for clongations factor Tu-mitochondria	Homo sapiens nuclear-encoded mitochondrial clongatation factor	P43-mitochondrial elongation factor homolog [human	lyq80b12,r1 Homo sapiens cDNA clone 202079 5'	H. sapiens GPx-4 mRNA for phospholipid hydroperoxidase	Human 22kDa smooth muscle protein (SM22)	yu59g01.s1 Homo sapiens cDNA clone 230448 3'.	yi57f06.r1 Homo sapiens cDNA clone 143363 5.	Human 4E-binding protein 1	H.sapiens EST sequence (011-118) from skeletal muscle	yl90g04.r1 Homo sapiens cDNA clone 45565 5.	Unknown	Human coupling protein G(s) alpha-subunit	Human UbA52 adrenal mRNA for uniquitin-32 millio acid	H. sapiens ESt sequence (003-63-10) than shorten	Human histone HZA.Z.
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			zc42d09,r1 Soares senescent tiploblesis totals
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		D52758	Human fetal brain cDNA 3'-end GEN-08/Avo.
		\neg	Human fetal brain cDNA 5'-end GEN-40/1/12.
HSO4187 1 0 17	12 6	M22490	Human bone morphogenetic protein-18 (BMI-1B)

		M27691 Human transactivator protein (CREB) mKNA, complete		0 X53743 H.sapiens mRNA for fibulin-1 C.	3 Z26328 H. sapiens partial cDNA sequence; clone HECU39	Z26328	U22055	10 R91724 Jyp98e02.rl Homo saplens cDNA clone 195482 5' simil	W51770 2248a02.rl Soares senescent fibroblasts NbHSr Homo	N42086 yy05b03.rl Homo sapiens cDNA clone 270317 5		\neg	7 F16507 H. sapiens ES1 sequence (147-02) Holli akurum mass	1	T	0 M38188 Human unknown projecti it citile prizery in the prizery i	0 Y00711 Human lactate dehydrogenase B (LDH-B).	5 D83174 Human collagen binding protein 2.	X70940	T30623	HUMGS0004747, Human Gene Signature, 3'-directed culvA	C01011 sequence.		M	7	П	\neg	\neg		D11838	-	T	135536 ES160931 noting suprens control and an analysis
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	117 CATGCGACCCCACGC	118 CATUTACARAN	_	119 CATGAICTIGAAAGG			121 CATGATCTTGAAAGG	122 CATGGTGGAGG1GCG	123 CATGGIGGACCCCAA		\$ DULUD VOOT DULL OF	124 CATGOACCAGGTGGG	125 CATGGGGGAGGGCT		A PACTITION IN A PACTION OF A PACTICAL PAC		127 CATGGAAAAA I I IAA	128 CATGGAICACAULL	129 CATGAGCCTTIGIIG	- 1	131 CATGAACAGAAGCAA						132 CATGIGITICAGGACC	CATCTACATAATGGC	153 CALOLOGO	114 CATGCTTAATCCTGA	134 CATGGGCAGAGAGCC	135 CATGRACTGA AGCC	200 000

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				\dashv	1	T	2310700 Home capiens cDNA clone 150596 3'.
137 CATGGATAGTTGTGG	H576495	0	<u> </u>	14	-	HU1094	7155811.51 Home sapiens cDNA clone 302319 3'.
			+	+	_		2892h06.s1 Homo sapiens cDNA clone 300059 3'.
	H765573	-	4	13	=	П	yv01e06.rl Homo sapiens cDNA clone 241474 5' simil
138 CATGGTGGTGGACAC			-				yi63g01.rl Homo sapiens cDNA clone 143952.5 simil
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2 ATCTOGGGTACCTT	H961304	0	9	13 2	6	1	yo31a05.rl Homo sapiens cDNA clone 179304 3.
139 CATOLOGO							2032005.FI Sources senescent trotoblests trottes. Trottes
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			-	_		R33196	yh77f08.r1 Homo sapiens culviv cione 132703 3.
	H1001313	E	12	13 8	2	104799	Human prothymosin-alpha
140 CATGITCALIALANI	H515821	-	┼-	13 8	12	D80012	Human KIAA0190 protein
	H125315	E	-	13 2	5	U02389	Human hLON ATP-dependent protease mixira
142 CATGACIGGCGAAG1	21,757,111		-	-	_	T29819	EST96617 Homo sapiens cDNA 5' end similar to A 1 r-u
	20170311	-	(*	13	9	X14850	Human histone H2A.X.
143 CATGGAAAGAGCIGA	CZ+07CH	-	+		-	104088	Human DNA topoisomerase [1 (top2) mRNA
144 CATGCAACTCTATGG	H269775	-	- -	2 2	+	1	Human beta globin retrovirus-like repetitive element
145 CATGAAATTTGGTGC	H16303		+	+	╁	1188396	EST28e05 Homo sapiens cDNA clone 28e05
	717071	F	-	-	∞	X74796	H.sapiens p85Mcm mRNA.
146 CATGCTGCACTTACT	H470114		+		-	D28480	Human mRNA for hMCM2, complete cds.
			+	╁	-	D55716	Human B lymphoma mRNA for P1cdc47, complete cds.
	00,000	-	-	12	=	╀-	EST14849 Homo sapiens cDNA 5' end similar to None.
147 CATGAATATTGAGAA	H33129		╬	+	╁	-	EST66942 Homo sapiens cDNA S' end similar to None.
				\vdash	+	T47475	yb14c03.ri Homo sapiens cDNA clone 71140 5'.
			+	╁	-	T50289	yb14h08.rl Homo sapiens cDNA clone 71199 5:
	HROUSTS	0	-	2	2 1		Unknown
148 CA G CACCAGGGGC	HK97495	0	2	13	2 7		Unknown
149 CATGGGGGCAGCG	H329737	0	9	12	4	U33818	Human inducible poly(A)-binding protein
	H1048113	0	2	12	4 12		Human HepG2 3' region cDNA, clone hmazcili.
151 CATGITITIONIANA	H977014	0	0	2	0		Human apolipoprotein A-II
152 CATOTOLOGAGAGA	H345789	O	2	12	5 4	249216	H. sapiens mitoxantrone-resistance associated unkivo.
IS3 CATGCCCACGGT AG	H67125	0	-	2	_		Unknown
154 CAIGAATICICCIAA	H 548203	0	0	12	0		Unknown
155 CATGGACCTCCGGGC	7901COH	, 0	7	=	7	M93651	Human set gene
156 CATGTGAATCTGGG1	ואקוחהי	,	-	1	1		

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	1004101	-	-		14 8	- 8	X15804	Human alpha-actinin.
157 CATGTCCTICTCCAC	2074001	,	╁	╁	 	╀	T19569	609F Homo supjens cDNA clone 609 similar to SET protein
158 CATGTATCTGTCTAC	H843483	0		╁	╁	╀	T	HHEA18W H. sapiens partial cDNA sequence; clone HEA18W;
159 CATGACGITCICITC		, ,	, ,	-	├	 -	08170704	zq73e07.r1 Stratagene neuroepithelium (#937231)Homo sapiens cDNA refore 647268 S. similar to TR:E16910 E16910 ENDONUCLEASE.;
160 CATGCCTGAGTCAG	H358581	1	٦,	- = =	3 6			2298h04.st Homo sapiens cDNA clone 300631 31.
161 CATGGAATTCCTCGA	H540023	1	1	+	+	+		zegodot.st Soares fetal heart NbHH19W Homo sapiens cDNA clone
						_	AA025809	366241 3'
		1	\dagger		-	-		2385h05.s1 Soares NbHTGBC Homo sapiens cDNA clone
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162 CATGGACGCCGAACI	11200011	,			-	-		zk84f04.st Soares pregnant uterus NbHPU Homo sapiens culna cione
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						~	A173819	AA173819 (clone 595100 5
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165 CATOTTOCOGAGGGG					-		H61710	yr24a07.s1 Homo sapiens cDNA clone 200190 3.
			T		_		H77330	yullf12.sl Homo sapiens cDNA clone 233319 3.
			\vdash	T	-	_	N69482	za18d05.s1 Homo sapiens cDNA clone 292903 3.
A Commercial A	21508115	0	-	2	4	6	H41078	yp52c11.s1 Homo sapiens cDNA clone 191060 3. simil
166 CATGGCAGACALIGA	CCCOCCU	,	 	9	├	0	H04630	yj49g03.r1 Homo sapiens cDNA clone 152116 5.
167 CATGCACTTGAAAA	1044674	> 0	. =	╁	+	-	R77027	yi66e12.r1 Homo sapiens cDNA clone 144238 5'.
168 CATGGGTTGGCAGG	CC+61/H	9	, -	╁╴	┨—	12	R32331	vh68g02.s1 Homo sapiens cDNA clone 134930 3' simil
169 CATGTTCCTCGGGC	H100/018	2	- -	2 5	+	: =	T86566	vd77g07.rl Homo sapiens cDNA clone 114300 5' simil
170 CATGCTGCCGAGCT	497192	9	٥١٠	2 2		2 -	\$77357	transcript ch 111 [human, RF1, RF48 stomach cancer c
171 CATGGTGAAAAAA	H753665	3	1	2 5	, ,	+	MILLIAR	Human spermidine synthase
172 CATGCTGTGCAGCA	H506149	5	0		1	-	1103011	Human mutator gene (hMSH2)
173 CATGTAGITTGTGG	-835515	3	-1	2	,	2 5	12950	11.man herenneneous nuclear ribonucleoprotein
174 CATGATGTAGTG	H242380	0	5	2	,	+	10000	Human lymphocyte activation antigen 4F2 large subunit
175 CATGGACCCACTACC	H545906	0	-	2	1	- -	CONCENT	Human fetal brain cDNA 5'-end GEN-108D03.
176 CATGAAATAGGTTIT	H12992	0	-	=	1	+	TK1071	whytem 1 Home sapiens cDNA clone 79035 5'.
					+	\dagger	DK1243	Human fetal brain cDNA 5'-end GEN-171G06.
					+	\dagger	N77240	yv44d02.r1 Homo sapiens cDNA clone 245571 51.
		4	5	5	1-	10	T35761	EST90898 Homo sapiens cDNA 5' end similar to EST c
177 CATGCCGGGCGTGGT	H371131			2	1	1		

H555168 0 8 10 3 3 T31901 EST40719 Homo sapiens cDNA 5' end similar to None.	1523bp	X98264 [HSMPP41 H.sapiens mknA for M-pitasy prospersion of the sapiens of the sap	Tabacan	0 4 10 7	Himan mRNA for KIAAU246 gene, partial cus	1 Little in the second	
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DILLE TO A COTO A COTT A COLUMNIA	78 CA100AC220C2	14 100000	179 ICATGAAACCCCAA1		DODOOD ACTION OF THE	(A)2000 A COCC COL	ていていていています。

Table 3 - Transcripts decreased in colon cancer

Transcripts decreased in only colon primary tumors

compared to normal colon (51 genes)

NC: Normal Colon
TU: Colon Primary Tumor
CL: Colon Cancer Cell Line
PT: Pancreatic Primary Tumor
PC: Pancreatic Cancer Cell Line

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Gene Name	The state of the s	Human mKNA for Dem-acum.	Human mRNA for cytoskeletal gamma-actin.	Himso mRNA for cytokeratin 18.	The state of the s	Human inputed in a mission down down professe (small subunit)	Human mKNA for calcium acpointed process (since)	H.sapiens CpG island DNA genoinic Mass. Lagueres, v.	zd30d02.rl Soares tetai near North 9 W Monto Suprim	Human fetal brain cDNA 5-eng GEN-1411502.	Unknown	Human thyroid hormone binding protein (p55) mRNA,	Sandalos 1 Homo sanieus cDNA clone 270345 3'	yyourday at the Seri I have NHHI 10W Home saniens	ZDUGAUD. II DOBICS ICIAI IMIB INTERIOR I TOTAL	Human inRNA for arginingsuccinate synthetiase.	Human mRNA for very-long-chain acyl-CoA dehydrogen	Human keratinocyte cDNA, clone 173.	human alpha-tuhulin mRNA. 3' cnd.	A A 341 K33 FST47188 Fetal kidney II Homo sapiens cDNA S' end	It capirus Id I mBNA.	H saniens mRNA for BiP protein.	Himan carochrome c oxidase subunit VIII (COX8) mRNa	Trullian Cylocan Complete C	Human Nat. All And State of Sand State of Sand State 153030 3.	Utgent of Homo sapiens cDNA clone 153030 5'.	Human Heart cDNA, clone 3NHC0642.
Agananan	Accession	X00351	X04098	4747001	A12005	D00017	X04106	Z65513	W61077	D60944		T0783	202707	N33042	W07627	X01630	1743682	T729146	1700557	_	\neg	٦-	\neg	104823	_	KS00350	C02981
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	C	185	120	2	245	36	38	42	26	26	1		3	2	56	57	; 5		8	2		<u>۾</u>	*	2	22	8	
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	-	# I ag seduence	1 CATGGCTTTATTIGE	2 CATCCTAGCCTCACG	A CONTROL A A CONTROL A		4 CAIGCIICAGCIAN	5 CATGCCCCAGIIUCI	6 CATGGAIGACCCC	7 CATGCTGTACAGACA	8 CATGCGGACTCACTG	o CATGCCCCGCGGAA	10 CATGCTGGAAGAGG	TL VUICE COLOR TO COLOR	II CAIGCCIOGCGTC	12 CATGAGCAGGAGCAG	13 CATGAACGTGCAGGG	14 CATGGCCGCCTGCA	15 CATGTGGGGAGAGGA	16 CATGGCTGCCCTTGA	17 CATGTGGCCATCTGC	18 CATGCGTTCCTGCGG	19 CATGEATCTGGTG	20 CATOGINA COTOCIT	21 CATGTAGCTCTATGG	2) CATGGTGCGTAGGG	

2 W52456 zc45e09.rl Soares senescent fibroblasts NbHSF Homo H671052 SI CATGGGATTCCAGTT

Transcripts decreased in both colon primary tumors and colon cancer cell lines compared to normal colon (130 genes)

NC: Normal Colon TU: Colon Primary Tumor

CL: Colon Cancer Cell Line pT: Pancreatic Primary Tumor

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97 zl92h02.s1 Stratagene colon (#937204) Homo sapiens cDNA clone	AA133597 512115 3 T53199 ya86605.si Homo sapiens cDNA clone 68552 3'.		3 6 M16364 Human creatine kinase-b mknA, compact contains Alu vf22e12.s1 Homo sapiens cDNA clone 127630 3' similar to contains Alu	10 4 R09410 repetitive element			R92735 contains Alu repetitive element	won374 cDNA clone 418222 3' similar to contains Alu repetitive element		181		9	32	130 M81457	15 C71047 HUMGS0002546, Human Gene Signature, 3'-directed CUNA		ECT	2168h06.81 Stratagene colon (#937204) Homo sapiens	AA054072 clone 509819 3*	zo18g08.si Stratagene colon (#93/204) notito septem 201	AA132736 5872943 similar to 5 w. LECG 100 100 100 100 100 100 100 100 100 10	- 1	84 2 X77658 H. saplens mKNA for then the content con ent con content con content content content content con content c	zo35c09.51 Stratagene colon (#557zo4) tronic zep	14 21 AA146606 588880 3	2022/2012 COST 2012 COST 2	2074g11.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone	AA161043 592676 3'
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		4947654	H284132	H368200						H501111	H350116	H1001401	H256186	H493039	H149715	H655433						H857781	11036717	11200001	H657337			
			17 CTAGTGCTCCTACCC		וווייייייייייייייייייייייייייייייייייי					20 CATGCTGGCCCTCGG	21 CATGCCCCTGGATC	22 CATGTTCACTGTGAG	23 CATGATTGGAGTGCT	24 CATGCTGACCTGTGT	24 CATGAGCAGATCAGG	26 CATGGGAAAACAGAA						O V O HO COOK	27 CATGTCACCGGICAG	28 CATGTGCAGCACGAG	AACTOTO	29 CA1000AAC		

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		-	-		-		2183f08.s1 Stratagene colon (#937204) Homo sapiciis Colon Civile	2
				•	_	AA08	AA088704 511239 3'	
	U404117.	4	32	54	09	40 H00427	27 yj23g11.r1 Homo sapiens cDNA clone 149636 5.	MA clone
30 CATGCGAGGGGCCAG	111111111111111111111111111111111111111						2063403,s1 Stratagene panereas (#93/208) flomo sapiens ceremonal	
						AAIS	AA158715 591557 3'	
		-	T	-	-	T08:	T08562 EST06454 Homo sapiens cDNA clone HIBBO31 3 enu.	ANA clone
		<u> </u>		l	-		zm21a12.s1 Stratagene pancreas (#93/208) homo sapiens Color	-
						AA07	_	
¥ 4 4 () Comm.	H790417	113	9	-	0	0 X73502		
31 CATGTAAATTGCAAA	1100010	E	36	48	45	43 J03191		
32 CATGGGCTGGGGGCC	70/000H	2 0	1 2	Ş	╁	111 U02629		
33 CATGGTGCTGAATGG	CC 10/H	3 6	3 5	1 2	╀	82 X07059		
34 CATGGTGCACTGAGC	H738243	3	2 ;	3 =	+	╁	-	
15 CATGTTTAACGGCCG	H1032614	≥ 	5	=	+	7	z174e07.st Stratagene colon (#937204) Homo sapiens cDNA clone	l clane
	6	200	7	r	L*	6 AA05	AA053660 510372 3' similar to contains Alu repetitive element	100,000
16 CATGCCCTCCCGAAG	H357729	2	=	+	+	τ	HUMGS04077 Human colon 3'directed Mbol cDNA, HUMGS040'7',	3S04077,
						D25711		
					-			cholloria
	11170765	105	~	22	4	27 Z56800		
37 CATGAGGTGGCAAGA	VO170011	3 8	: =	0	┼	┨	174 Human guanylin mRNA, complete cds.	
38 CATGATACTCCACTC	11407071	1 5	25	2	4	16	Unknown	CD-74781
39 CATGCTCGCGCTGGG	1024041						yn01601.r1 Homo sapiens cDNA clone to 1113 5 similar to 51.23.rd	J. CD / N. 7. 1C
	HK97514	82	32	28	37	65 R90	R90863 CE00760;	
40 CATGGGGGCAGGCC	11071701					172/		
	2573666	gg	33	42	28	87 X9:		
41 CATGGAAGCAGGACC	0998860	75	22	28	e	.9X 9I	X67325 H.sapiens p27 mRNA.	
42 CATGCCAGGGAGAA	JI COCH	74	31	R	2	31 F10	F16604 H.sapiens mitochondrial EST sequence (0091.46) 110111	contains Alu
43 CATGACACAGCAAGA								
	H134304	69	29		3	9N 0	N69361 repetitive element; contains element L. I repetitive element	clone
44 CATGAGAATAGCTTG							ze30b10.st Soarcs retina NZD4FIR right Squares	
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	40000000					H2	H26689 repetitive element contains 1 Ani repetitive cleme 681957 3	681957 3'
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45 CATGCGCTGTGGGGT	H424875	88	6	9	5	23 JAPA	0000) Silling to the contract of the contract	

 W47357 clone 3.24710 3	-	\neg	R07159 [yf13h12.s1 Homo sapiens cDNA clone 120791 3.	L02785 Homo sapiens colon mucosa-associated (DRA) mKNA	U11862 Human clone HP-DAOI diamine oxidase	N93240 zb68b06 s1 Homo sapiens cDNA clone 308723 3'.	NIB1986 Normalized infant brain, Bento Soares Homo sapiens cDNA	T16906 3'end.	H78256 SP:SBP MOUSE P17563 SELENIUM-BINDING	EST47523 Homo sapiens cDNA 3' end similar to stinual to Scientification	 V00493 Human messenger RNA for alpha globin.	Unknown	X51346 Human jun-D mRNA for JUN-D protein.	R34039 yh83f04.r1 Homo sapiens cDNA clone 136351 5.	[10396] [vj44e07.s1 Homo sapiens cDNA clone 151620 3].	-	z171e06.rl Stratagene colon (#937204) Homo sapiens cDNA clone	AA053043 510082 5'	F17394 H.sapiens mitochondrial EST sequence (UU/113) Itom	Z13009 H.sapiens mRNA for E-cacherin.	X15505 Human mRNA for pancreatic trypsinogen III.		M20469 Human brain-type clathrin light-chain Universe,	yy92c07.st Homo sapiens cDNA clone 281004 3 Similar to Contains and yy92c07.st Homo sapiens element MER32 repetitive element	1	1	U11716 vm14fff6 1 Homo saniens cDNA clone 47991 5'.	_	740539 ye05b02.s1 Homo sapiens cDNA clone 60555 3.
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					46 CATGCATAGGITTAG	47 CATGGCCGACCAGGI	48 CATGAGCTCTTGGAG				100000	49 CATGCCCAACGCGC	50 CATGGACGCGCCCC	51 CATGACCCCCCCCCC	52 CATGATGCGGGAGAA				S3 CATGICAGCIOCAAC	SA CALGGIAACIOIACI	SS CATGIGIGGIGGIG	S6 CATGGCIGIGCCIGG	S/ ICATGLICACIONOCACO	S8 CATGGGC1GGGC1G	59 CATGTAATCCCAGCA	60 CATGGACCAGTGGCT	61 CATGGGCACCGTGCT	62 CATGAAGGACCTITT	

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63 CATGGCAGCTCC1G1	בטינינים	:					N20325 yx44c11.s1 Homo sapiens cDNA clone 284320 3
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64 CATGTGCCTGGTTC	H972720	2	2	1	+	+	1
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65 CATGACAAACCCCA							***********
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66 CATCLACCATOCOCO	H126619	41	7	_	4	33	Unknown
67 CATGACTOTOCOCOC							Zp4411.51 Stratagene interest 22.22.22.22.22.23.23.23.23.23.23.23.23.2
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68 CA1001ACACACA							_
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69 CATGAATCACAAAIA	1133300						2 67e0 .s Stratagene colon (#93/204) 110110 saptens CO. 110110
and different							_
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71 CATGCCAAAGCTATA 72 CATGCGGGAGTCGGG 73 CATGGCCGTGGAGGC 74 CATGCCCCCGAAGCC 75 CATGCCCCCGAAGCC 76 CATGCCCCCCAAGATG 76 CATGGCCCAGTGGCT	H328308 H434907 H618121 H349706 H259108 H611050	38 1 33 38 1 37 37 37 37 37 37	23 - 6 9 8 - 6	22 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 10 0 2 0 18	 	Human CO-029. ym89c10.s1 Homo sapiens cDNA clone 166098 3'. H.sapiens Irp mRNA. Unknown Human carbonic anhydrase II mRNA, complete cds. Unknown Unknown Humsoriptional regulator mRNA
77 CATGATGATGAGAA 78 CATGCCTGCCCCCT 79 CTAGTGGAAAGTGAA 80 CATGGTCATCACCAC 81 CATGCTTATGGTCCC 82 CATGCTGGCCTCTG	H241323 H386190 H950457 H740629 H511670	╀╀┼┼┼				X60188 V01512 U34279 AA287021 T55226	X60188 Human ERK1 mRNA for protein serinc/threonine kinase V01512 Human cellular oncogene c-fos (complete sequence). U34279 Human uroguanylin mRNA, complete cds. U34279 Human uroguanylin mRNA, complete cds. AA287021 zss7c03.s1 Sources NbHTGBC Homo sapiens cDNA clone 701572 3' yb47a01.s1 Homo sapiens cDNA clone 74280 3' containing L1 y55226 repetitive element y55226 repetitive element y55226 repetitive element y556610.s1 Homo sapiens cDNA clone 26129 3' similar to gb:X07173 y156610.s1 Homo sapiens cDNA clone 26129 3' similar to gb:X07173
83 CATGGCCCAGGGCCC 84 CATGTTTTTACTGAT	H610982 H1047673	33	mr.	00	2 2 2	AA40618 R09752 R81530 T32348	AA406180 2u65c08.s1 Soares testis NHT Homo sapiens cDNA clone 742862.3' R09752 Unknown R81530 yj02b10.r1 Homo sapiens cDNA clone 147547.5'. T32348 EST472.i1 Homo sapiens cDNA 3 end similar to None. zd17g02.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 247e12.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone
85 CATGCCTGCTTGTCG 86 CATGACCTGGGGAGG 87 CATGCCTTCAAATCA 88 CATGTCGGAGCTGTT	H387054 H96931 H390158 H893564	31 32 33 33 30	7 9	-4 04	0 8 8 9 1 1	AA398527 6 X63187 6 R46266 1 H98618 1 AA171703	50

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89 CATGGGAGGIGGGG	171003970	30	-	-	16 17		T30344 [gb]U53204[HSU53204 Human piecum (TLLC1) mixin 1, compression 130344 [gb]U53204[HSU53204 Human piecum (TLLC1) mixin 1, compression 120344 [gb]U53204
90 CATGTICCACIAACC	1752207	200	-	F.	9 3	_	yc22a06.s1 Homo sapiens curve cione o 1354 5.
91 CATGGTCTGGGGGA1	177771		+	\vdash			gblu67963 HSU67963 Human lysophospholipase nonlong (110-12)
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92 CATGITAACCCCTCC	H984414	7		+	+	+	7
7,						R69445	
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						R79191	
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						R49965	
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							TIMORS
	H231029	28	2	2	4	6 AA41094	1 ESTICOLDAY COMP 15120 S.
93 CATGAIGACGCICAC						H02520	_
				-	_		zo12g08.rl Stratagene colon (#ys/204) molino sapiralis colon in
							586718 5' similar to TR:G459890 G459890 OVEKEXPRESSED III
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94 CATGCACCTGTCATC	H286420	28	7	\$	1	+	1
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95 CATOONICCONNEIS							
Topody	H510123	27	_	Ş	6	6 H43742	2 EZRIN
96 CAIGCLIAGAGGGG	H778975	27	4	3	_	0	_
97 CATGATGGCCCAIAC	14501884	27	-	0	7	0 V00497	7 Human messenger KNA tor peta-gloom.
98 CATGCCAAGAAGIG	11371001						

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119 CATGTTTCTCGTCGC	21.07013	*	1-	-	_	0	_	
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125 CATGGCTTGGGGAT1	ממכריהם	-	+	+	-			yc36e02.rl Homo sapiens cDNA clone 62110 J Shintan to Borger
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126 CATGACCCAACIGCC	11/01/894	2	0	0	7	2		go 193613(1930) John Sapiens
127 CATGCTGAACCICCC	1147707		+	-				zr[95][.s] Stratageno N L neuronal precursor, 12123 : 1213
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128 CATGCAAGAGITTCT	1771177		+	+	\dagger	-		zq97h01.s1 Stratagene N12 neuronal precuisor 23.220 110110 32press
			,			<u> </u>	V218730	AA218730 CDNA clane 649969 3'
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	01363610	=	0	0	co	2	H38178	TUMOR-ASSOCIATED ANTIGEN L6 (HUMAN);.
129 CATGGTCCGAGTGCA	01002/11		c	ç	6	0		Unknown
TAPICATGTTTGGTTTCAC	H1043445		7	,	,	•		

cell lines compared to normal colon (78 genes) Transcripts decreased in only colon cancer

NC: Normal Colon
TU: Colon Primary Turnor
CL: Colon Cancer Cell Line
PT: Pancreatic Primary Turnor
PC: Pancreatic Cancer Cell Line

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	W15552 [2b91h11.s1 Soares parathyroid tumor NoHPA Homo sap		F10326 Imuscie EST186995 HCC cell line (mutastasis to liver in mouse) II Homo	AA315049 sapiens cDNA S' end	F01150 H. sapiens partial cDNA sequence; clone A6A03; ver	N29971 [yw53h01.s1 Homo sapiens cDNA clone 255985 3].	K02883 Human MHC class I HLA-A2 gene, complete cds.	R09140 y225f12.s1 Homo sapiens cDNA clone 127919 3'.	R76005 yr22c10.s1 Homo sapiens cDNA clone 158994 3'.	T33596 EST58371 Homo sapiens cDNA 3' end similar to None.	F16449 H.sapiens mitochondrial ENI sequence (129-09)	ZZS4f10.51 Soares ovary (umor Ivorio) 1 (10)110 September 20101 Company of 172 (1970)	Section Services Course thrown NAHOT Homo septens CDNA clone	AA292466 723956 5' similar to TR:G205858 G205858 RAT ORF	zb62d07.51 Soares fetal lung NbHL19W Homo sapiens cLNA clone	308173 3' similar to PIR:A39484 A39484 androgen-withdrawal	N92384 apoptosis protein RVP1, prostatic - rat	2b19c06.s1 Homo sapiens cDNA clone 302506 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVP1,	N80203 prostatic - rat;	zk39d06.s1 Soares pregnant uterus NbHPU Homo sapiens cUNA	clone 485195 3' similar to PIR: A39484 A39484 androgen-	3		M34088 Human episialin variant A mRNA, 3' end.			\neg	1.27415 Homo sapiens huntingtin (HD) gene, exon oo.	ne organature,	1 - 1
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08Z179H	H687915		H69669H	0951707	50C107H	H294400	1132508	11400017	H409077		H609624		H610922	07673011	H320000								H175872	H387596	H188027	09/25EH	H2235	HK07977		H167659
Г		בין כאומתכרוו אמממע	CATGGGGGTCAGGG		29 CATGATTTTCIAAAA	\neg	_	\neg	33 CATGCTCTGCCCIC		TIJJJJTYJJJJTYJ	יייייייייייייייייייייייייייייייייייייי	15 CATGGGGGGGG		36 CATGTGGCGCGIGIC										-	\neg	_	_	42 CATGGCCACGTGGAG	43 CATGAGGATGTGGG

zo80f04.s1 Stratagene ovarian cancer (#937219) Homo sapiens	H838494 20 7 1 3 4 AA411012	AA133595	2156b12.51 Soares ovary tumor NbHO1 Homo sapiens CDNA chone AAA93774 726335 3'	H710520 20 7 2 2 2 R53216	. H240121 19 4 0 3 3 DZ0113	H496981 19 5 0 1 4	H1013522 19 4 1 8 2	H33355 18 4 2 2 8 K81/6/	H183018 18 131 2 17 / D31021	H77551 18 3 3 70 1 M11465	T H655547 18 13 3 /0 1 278188	H32926 17 4 0 0 0 M22406	TOSE 0 0 0 0 C C C C C C C C C C C C C C C	H14470/ 1/ 16 0 0	N79237 PIR:S49589 S49589 cortical granule lectin - African clawed frog :-	T3 1354 (EST30893 Homo sapiens cDNA 5' end similar to None	15 A 0 0 H54696	H322430	11293000 16 A 2 B 1 AA374631 EST86866 HSC172 cells I Homo sapiens cDNA 5' end	H034970	AA137163 cDNA clone 565790 5'	2k10f05.s1 Soarcs pregnant uterus NbHPU Homo sapiens cDNA	21	DCATTGA H948543 15 2 0 1 0 D25681 Human colon 3'directed Mbol CLINA, HOM D30-00-1, Cloud Signature 1, Cloud	AA253331 3'	H05110 Jy175f07.s1 Homo sapiens cDNA clone 43778 31.	H341720 15 8 1 1 10	H341/20
	TOTOTE	44 CA101A1A1A1A1A1A1A1A1A1A1A1A1A1A1A1A1A1A			45 CATGGGTTGGTTGAT		7	_	_	CATGACAGTGTGTGT	52 CATGGGAAAAGTGGT		54 CATGACACCCATCAC	55 CATGAGATCCCAAGG				56 CATGAATAGTTTCCC		58 CATGGCTTTGCTTTG				SO CATGIGGEGCATIGA			-	60 CATGCCATCGICCII

M25629 Human kallikrein mRNA, complete cds, clone clone p	H18836 ym45d10.s1 from Sapiens CDIVI Come sapiens CDNA	zkolejuki Soares pregnam utatus kutut Ortania arpina zakoren arpina arpina zakoren arpina zenen arpina zene	AA026974 Clone 409220 3	zulZcjZ.rl Soares (csns ivn i nomo sapiems views	similar to gb:M61900 Human prostagiandin U syntnase gene,	A A 405031 complete cds. (HUMAN);	gblU66894 IISU66894 Human epithelium-restricted Ets protein ESX	1166894 mRNA.	Т	U73843 mRNA, complete cds	D25996 Human colon 3'directed Mbol cDNA, HUMGS06772	1	ze88g07.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone	AA071520 366108 3'	za90h10.s1 Soares fetal lung NbHL19W Homo sapiens cDNA clone	N90742 [299875 3.	zn52h06,s1 Stratagene muscle 937209 Homo sapiens CDINA Clone	AA086292 561851 3'			774426 yc82e01.r1 Homo sapiens cDNA clone 22300 3.	N73771 za61h02.s1 Homo sapiens cDNA clone 29/U/5 3.	zh75f08.s1 Soares fetal liver spleen INFLS SI Homo sapiens CO.	W90388 clone 417927 3'	F03786 H. sapiens partial cDNA sequence; clone c-27006.	U14631 Human 11 beta-hydroxysteroid dehydrogenase type 11	ya31a06.s5 Homo sapiens cDNA clone 62194 3' contains Atu	T41121 repetitive element,	Unknown		Z58486 Unknown	Unknown
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2 CATGGGGCTACGTCC	\top	CATALCECCOCC							64 CATGAGGTACTA			65 CATGCAAATAAATTA	1	1	67 CATGGTTCAATCCCT	7			Live Control				71 CATGGGTGGCCCGGG				72 CATGTACTIC		- 1			76 CATGGCGGCGCIC

v68073 343318 3' similar to contains Alu repetitive element; 0 0 0 Ξ H874226 78 CATGTCCCCGTTACA

Table 4 - Transcripts increased in pancreas_cancer .

S.A.G.E. Tags elevated only in Pancreatic Tumor

Nr. Normal Colon

Tin Colon Tumor

CC Colon Cancer Cell Line

PT Pancreatic Tumor

1	Cell Line
Talleleant June	PC: Pancreatic (
<u>-</u>	D

																	_	-	_	-		1.		1-		_		i
Can Name	who should be sapiens cDNA clone 137455 3'	2205603 s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone	490541 3'	zk51c03.s1 Soares pregnant uterus NbHPU Homo sapiens culve cione	486340 3'	2133c08.81 Soares pregnant uterus NbHPU Homo sapiem CDIVA CIOMA	503726 31	zo71h12,s1 Stratagene pancreas (#93/200) mino saprem contraction	592391 3' Clore 776174	zt54e04.81 Soares ovary fumor Norto I nomo sapiems contractions	3' Stratagene	zo78c07.s1 Stratagene pancreas (#93/206) Honno 20/000/.s1 Stratagene	pancreas (#937208) Homo	1970h01 s1 Homo sapiens cDNA clone 154129 3'	Hoging of Homo saniens CDNA clone 79335 3'	Tr	H. Sapicus interest of cytostates	H sapiens spasmolytic polypepting (ar) markets	za61d12.51 Homo sapiens cDNA clone 29/04/2	zv16g01.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753840.5		2v16g01.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 753840 3	2186g12.s1 Stratagene colon (#937204) Homo Sapiens Colon Citatagene	31 Cone 587358 Homo sapiens cDNA clone 587358	2019e04.61 Stratagend colon (#7.1.204) Managend Stratagend	3' Standard and other in cell 937223 Homo sapiens cDNA clone	2044900,s1 SualaBuit directions	3637.1.4.3
Accession	Accession	COCOCY	AA126719		AA044296		AA131586		Examples AA157983		AA292929		A A 1 59306	1064017	770407	105330	X52426	X51698	N70419	AA411599		AA410508		Examples AA115723	!	AA132875	74,744	AA147677
		Examples K30303							Examples								Examples X52426	Examples X51698	Framples N70419					Example				
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DO Dancestic Cell Line	Tag Semience	1 CATGAAAGCAAACCA								2 CATGAAAGCAGTTTA								3 CATGAAAGCGGGGCT	4 CATGAAATCCTGGGT	SCATGAAATGGACAAC					6 CATGAACCAGTTTGT			
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zq81h12.s1 Stratagene hNT neuron (#937233) Homo sapiens cDNA clone	83	AA412071 2165h12.81 Soares testis NHT Homo sapiens cDNA clone 727271 3' N63154 yz37f12.81 Homo sapiens cDNA clone 22603 3' 187236 yc81h04.81 Homo sapiens cDNA clone 22603 3'	22			944858 3' similar to SW:CUIA_ECOLA FOOD TOTAL DIVALENT CATION TOLERANCE PROTEIN CUTA TOTAL STATE STATE STATE TO STATE TO STATE	yi95e05.s1 Homo saptens curve care reported to SP.CYCY_ECOLI P36654 C-TYPE CYTOCHROME BIOGENESIS R72650 PROTEIN CYCY	AA181976 DIVALENT CATION TOLERANCE PROTEIN CUTA Human phosphotyrosine independent ligand p62 for tthe Lck SH2 domain		==	D00422 Human sphingolipid activator protein 1 mRNA 103015 Homo sapiens sphingolipid activator protein 1 mRNA	M60255 Human mutant cercutosito serves	2375 yw37d01.s1 Homo sapiens cDNA clone 254401 3'	43
	H30689 3 7 13 13 17 Examples R51318 135270	H31221 7 6 8 6 130 Examples N63154 187236	To Committee	=	H36183 5 10 14 12 23 Examples recent	W70	R77	V	1	10 9 18 31 27 Examples	00 00 00 00 00 00 00 00 00 00 00 00 00		0 !	
	7 CATGAACTCTTGAAG	8 CATGAACTGCTTCAA) CATGAACTTGGCCAT	IN CATGAAGATCCCCGC					11 CATGAAGGGAGGTC			11 CATGAATGAAAAAA	14 CATGACAAACTGTGG

		AA279290	2584a06, s1 Soares NbHTGBC Homo sapiens cDNA clone 704146 31
		A A 0 4 6 2 5 3	21/2a/2.81 Soares read near 1.05 2.1. 376682 3'
	H67396 2 7 7 16 37 Exam	Examples Z58016	H.sapiens CpG DNA, clonc 26c7,
15 CATGACAACTCAATA		AA151668	zo29e02.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 588290 3' similar to SW:BI3 MOUSE P28662 BRAIN PROTEIN I3
			za07c06,r1 Soares melanocyte 2NbHM Homo sapiens cDNA cione 2318/7
		W02958	5/ 2070-05, s. Stratugene pancreas (#937208) Homo sapiens cDNA clone
	H71151 0 1 0 2 14 Exam	Examples AA1556464 592256 3	592256 31 Source ferral heart NhHH 19W Homo sapiens CDNA clone
16 CATGACACCC1 61 92		AA025673	2690nuy.si Suates retained incara inc
		N70895	za89h12.sl Homo capiens cDNA clone 299783 3
	0 0 4 13 4	Examples X02491	Human interferon-inducible mRNA (cDNA 9-27): membrane
17 CATGACCATTGGATT		J04164	Human interferon-inducible protein 9-27 mkNA
		X84958	H. sapiens mRNA for interferon-induced 1 / KDa mennota
	1100050 1 4 2 13 7 Exan	Examples X56841	H. sapiens HLA-E gene.
18 CATGACCCTTTAACA		X64879	H. sapiens mRNA for H.AE neavy chain (canus 4 - 1)
	1101579 49 22 45 70 94 Exan	Examples M21186	Human neutrophil cytochrome o ugai cuant pzzw
19 CATGACCGCCGTGGT		M61107	Human p22-phox (CYBA) gene, exous 3 and 4
	H97158 0 3 0 28 17 Exar	Examples D00244	Human Pro-urokinase gene,
10 CATGACCTGTGACCA		K02286	Human urokinase gene, 5 cho
		M15476	Human pro-urakinase mikhe, compiece cas
		12.17 00025	Himan myotonic dystrophy kinase (DM kinase) gene
21 CATGACGCCCTGCTC	H103912 0 1 0 11 2 EXE	Examples Luog32	Homo saplens myotonin protein kinase (DM) mRNA
17	000	Examples H44451	yo75f06.s1 Homo capiens cDNA clone 183779 3'
22 CATGACGTGGTGATG	24		2042[07.5] Stratagene endothelial cell 937223 Homo saptens CDNA Crouse
		AA157329	KD PROTEIN
			2631g06.s1 Source senescent fibroplasts Notice round septimis Control 2017/10/2019 10/
		W46455	KD PROTEIN

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11 12 13 14 15 15 15 15 15 15 15			F		r			X12454	Human mRNA for vascular anticoagulant
CATGATCAAGAATCC H213518 2 1 5 25 1 Examples 103909 CATGATCAAGGGTGT H213679 12 9 25 12 156 Examples 103909 CATGATCAAGGGCCA H213751 0 2 8 3 10 Examples L42856 CATGATCGACCAAAGGC H225502 1 0 0 17 4 Examples L42856 CATGATCGAAAGTTCGTT H243676 0 0 1 0 14 Examples L42856 CATGATCGTAAACGA H24487 0 4 5 44 94 Examples M35633 CATGATGTTTTTTT H244487 0 4 5 44 94 Examples M3563 CATGATGTTTTTTTT H286424 0 4 2 10 1 Examples D78203 CATGATGTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT			+	\bot	T	T	-	Γ	Juman placental anticoagulant protein (PAP) mRNA
CATGATCAAGAATCC H213518 2 1 5 25 1 Examples 103909 CATGATCAAGAATCC H213518 2 1 5 25 1 Examples 103909 CATGATCAAGGGTGT H213679 12 9 25 12 156 Examples 100953 CATGATCAAGGTCT H213750 16 7 14 12 40 Examples L42856 CATGATCAACTTCGA H229502 1 0 0 17 4 Examples L225242 CATGATGATGAAACTTCG H23531 2 3 12 3 22 Examples L24774 CATGATGTTTTCT H243676 0 1 0 14 Examples L25820 CATGATGTTTTCT H244487 0 4 5 44 94 Examples L3457 CATGATGTTAAAGC H270083 0 1 2 10 Examples L32620 CATGATGTTTAAAGC H270083 0 1 2 10 Examples L32620 CATGATGTTTAAAAC H27083 0 1 2 10 Examples L32620 CATGCACCTCAATAAAA H291889 0 0 2 3 19 Examples D78201 IGAGGGTGTTAAAAAA H291889 0 0 2 3 19 Examples D78201 IGAGGGTGTTAAAAA H291889 0 0 2 3 19 Examples D78201 IGAGGGTGTTAAAAA H291889 0 0 2 3 19 Examples D78201			+			Ī	4		Juman Lipocortin-V mRNA, complete eds
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CATGATCAAGTTCGA H219750 16 7 14 12 40 Examples L42856 CATGATGAAACTTCG H229502 1 0 0 17 4 Examples L42856 CATGATGAAACTTCG H229502 1 0 0 17 4 Examples L42856 CATGATGATGAAACTTCG H23531 2 3 12 3 22 Examples Z25820 CATGATGATGTCTTCGTT H243676 0 0 1 0 14 Examples M84711 CATGATGTCTTTCTT H243676 0 0 1 0 14 Examples M84711 CATGATGTCTTTTCT H24487 0 4 5 44 94 Examples Z33457 CATGATGTTAAAGGA H24487 0 4 5 44 94 Examples Z33457 CATGAACTTAAAAGC H270083 0 1 2 10 1 Examples N23207 CATGCACCTGAATAAA H291889 0 0 2 3 19 Examples D78203				<u> </u>	1	=	Ryamules		zm03a05.s1 Stratagene corneal stroma (#937222) Homo sapiens CDNA. slone 513008 3'
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CATGATGTCTTCGTT H2430/D U 1 2 1 14 2 Examples M62403 CATGATGTCTTTTCT H243710 1 2 1 14 2 Examples M62403 CATGATGTGTAACGA H244487 0 4 5 44 94 Examples Z33457 CATGATGTGTAACGA H270083 0 1 2 10 1 Examples N23207 CATGCACCTGACTTAAACC H270083 0 1 2 10 1 Examples AA285023 CATGCACCTCAATAAA H291889 0 0 2 3 19 Examples D78203		7470707			1	14	Evamples		40S RIBOSOMAL PROTEIN S3A (HUMAN)
CATGATGTTTTCT H243710 1 2 1 14 2 Examples 733457 CATGATGTGTAACGA H244487 0 4 5 44 94 Examples 723457 CATGATGTAACGA H270083 0 1 2 10 1 Examples N23207 CATGCAACTTAAAAC H286424 0 4 2 10 1 Examples AA285023 CATGCACTCAATAAA H291889 0 0 2 3 19 Examples D78203	CATGATGTCTTCGTT	H243676	\perp	7 7	7		Deample	T	Human insulin-like growth factor binding protein 4
CATGATGTGTAACGA H24487 0 4 5 44 94 Examples Z33457 CATGCAACTTAAAGC H270083 0 1 2 10 1 Examples N23207 CATGCACCTGTCCTT H286424 0 4 2 10 1 Examples AA285023 CATGCACTCAATAAA H291889 0 0 2 3 19 Examples D78203	1 CATGATGTCTTTTCT	H243710	+	7	47	7	Transferan		Human insulin-like growth factor binding protein-4 (IGFBP4) gene,
CATGATGTGTAACGA H24487 0 4 5 44 94 Examples Z33457 CATGCAACTTAAAGC H270083 0 1 2 10 1 Examples N23207 CATGCACCTGTCCTT H286424 0 4 2 10 1 Examples AA285023 CATGCACTCAATAAA H291889 0 0 2 3 19 Examples D78203									promoter and complete cds
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H286424 0 4 2 10 1 Examples AA285023 M33680 H291889 0 0 2 3 19 Examples D78203	4 CATGCAACT DAMAGC		-	_	1				2125611.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 714188
H291889 0 0 2 3 19 Examples D78203		H786424	0			-	Examples		3' similar to gb:M33680 CD81 ANTIGEN (HUMAN)
H291889 0 0 2 3 19 Examples D78203	SCATGCACCIGICCII	7.00411	+	1_				VI33680	CD81 antigen
[16280]	Adamachana	HZ91889	0			19	Examples	578203	Neurosin
	CAT GCACT CANTAGO		+	\perp				362801	protease M

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				- 0	Examples AA149942	A149942	2068d04.s1 Stratagene parcreas (#937208) Homo sapiens cDNA clone 592039 3' similar to TR:E218488 E218488 TRYPTASE
17 CATGCAGCCTGGGGC	HJOOFH	1					zp66b09.r1 Stratagene endothelial ceil 937223 Homo sapiens cDNA clone
						3	625145 5' similar to gb:M16937 HOMEOBOX PROTEIN HOX-B7
18 CATGCAGCGCGCCT	H301462	4 11 12	2	71	Examples AA187553 M16937	AA187553 M16937	(HOMAN), contains eventum. Homechox protein HOX-B7
	20110011	c	0	12	No Match		
19 CATGCAGGTTGTCCT	H307170	5 1		1.1	Examples U14972	114972	Human ribosomai protein S10 mRNA
50 CATGCAGTCTCTCAA	H309109	7 0	\perp	= ==	Examples U27293	327293	Human leukotriene A4 hydrolase gene
51 CATGCATCCCGTGAC	H316857	1	L	+		103459	Human leukotriene A-4 hydrolase mRNA, complete cas
		+	-	\vdash		102959	Human leukotriene A-4 hydrolase mknA, comprete cus
	DROSCELL	0	5 13	6	Examples X82434	K82434	H. sapiens mRNA for emenn
52 CATGCATTCCTCCTT	11223138	1	1_	7	Examples M88338	V(88338	Human serum constituent protein (Macaa) muana
S3 CATGCCACCCCACC		=	1	56	Examples U14971	J14971	Human ribosomal protein by marker and the marker
54 CATGCCAGTGGCCCG	_	1	1	2	Examples L01697	76910	Homo sapiens alpha-1 type X v collagen max.A
SS CATGCCATTTTTGG	1	2 0	18	4	Examples X54079	X54079	Human mRNA for heat shock protein fish 2.0.
56 CATGCCCAAGCTAGC	11204401		1_	-		223090	H. sapiens mRNA for 28 kDa near snock protein
		-		-		X16477	Human mRNA fragment for estrogen-regulates, 274 process
		+	1			S74571	estrogen receptor-related protein=27-kna near bittorn protein
	i	151	43 19	डि	Examples X69392	X69392	H. sapiens mRNA for ribosomal protein L.20.
57 CATGCCCATCCGAAA	H34/402			1		L07287	Human ribosomal protein L26 (RPL2b) gene
	1750000	-	6 14	25	Examples U40434	U40434	Human mesothelin or CAK1 antigen precursor nucky.
AN CATGCCCCCTGCAGA	Concern			-			Human mRNA tor pre-pro-megakaryocyte potentiam
						D49441	(CUS)
East	H353481	0	8 0	11	Examples U12819	U12819	Human plo-ting (plo) Bene
SO CATGCCCCCATAGAL						U38945	Human hypothetical 19,1 KDa process (Constitution of Interpretation of Interpretatio
						569804	n16
			1	+		569877	CDK41 cyclin-dependent kinase 4 inhibitor
		†	1	1			tumor suppressor gene, P16/MTS1/CDKN2=cell cycle cycle negative
	•					878535	regulator beta form
	C)023	6	7	34	Examples Z47319	247319	H. sapiens mRNA for expressed sequence tag (clone 21ff7119)
(1) CATGCCCTCCTGGGG	H357807	9					

						A A 398406	2160h12.s1 Soares testis NHT Homo sapiens cDNA clone 726791 3'
	2000		14	100	Examples U21049		Human DD96 mRNA
61 CATGCCGGCCCTACC	H370034	7 7	: 8	8	Examples X03212		KERATIN, TYPE II CYTOSKELLIAL /
62 CATGCCTGGTCCCAA	CTC (BCI)	1	-			7576164	2p/3101.s1 Stratagene neck cen as 75720 assess september 675840 31
			\dashv	$\frac{1}{1}$	1	1410/02/	2035g11.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 611492
	00000	3	- 2	23	Examples AA176457	AA176457	3' similar to TR:G663269 G663269 BOLA
63 CATGCCTTTGAACAG	H392/09	1	+	+			zp35e11.s1 Stratagene muscle 93/209 Homo sapicus Company company
						AA176541	3' similar to TR:G663269 G663269 BULA.
	11115041	21 13 45	75	-	Examples X02492	X02492	Human interferon-inducible mKNA tragment
64 CATGCGCCGACGATG	1413014	15	9	12	Examples T53402	rs3402	ya88g05,s1 Homo saptens culvia clone do 72. 3
65 CATGCTCAACAGCAA	Tato (11)			-			2 Come fetal heart NhHH19W Homo sapiens cDNA clone
,					•		224 / guo. St. Soares Actin 1900 September 1900 Sep
	-					W69493	343638 3 Billina 10 1 Acceptor related protein
	STAFFALL	1 4 2	23	1	Examples X13916	X13916	Human michael Louis and Committee Co
66 CATGCTCAACCCCCC	200000	ľ		18	Examples X80335	X80335	H. sapiens (24) Ferritor in passion galaxie.
67 CATGCTGAGAAACTG	H495370		1,	=	Examples X04828	X04828	Human mRNA for G(1) protein alpha-suounn
68 CATGCTGAGTCTCCC	#C#####	7 00		1	Examples U14966	U14966	Human ribosomal protein L5 mKNA
69 CATGCTGCTATACGA	H498887		1.	=	Examples T90665	T90665	yd41g08.s1 Homo rapiens cDNA clone 110846 3
70 CATGCTGCTGAGTGA	H499247	7		+			EST43791 Fetal brain I Homo sapiens CDNA 3 end similar to storous
						AA338799	hormone receptor hERR1
		1		\dagger		H97236	yv98b06.81 Homo sapiens cDNA clone 250/39 5
		1		1=	Evanules C14084	C14084	Human fetal brain cDNA 31-end GEN-018D10
7 CATGCTGGCGCCGAT	H501337	3	1	3 3	December 100017	510001	Human lipocortin II mRNA
72 CATGCTTCCAGCTAA	H513181	2	2 2	=	Framples Z19574	Z19574	H. sapiens gene for cytokeratin 17.
73 CATGCTTCCTTGCCT	H514022	7	4 02	+	- Commission	X62571	H. sapiens mRNA for keratin-related protein
		+	1	+		X05803	Human radiated keratinocyte mRNA 266
	0010011	,	15	4	Examples X79067	X79067	H.sapiens ERR-1 mRNA 3' end.
74 CATGUTTACTTCCT	W277198		L	37	Examples X51779	X51779	Human mRNA containing an Ain repeat
75 CATGGANAAAAAA	H524289	1 .		-		X82240	H.sapiens mRNA for Teell leukemia/lymphoma
	11525249	F	14 8	S	Examples V00572	V00572	Human mRNA encoding phosphoglycerate Kinase.
76 CATGGAAACAAGATG	OHECTCH	-	1			D29018	Human keratinocyte cDNA, clone uot
						1,00160	Human phosphoglycerate kinase (pgk) auctor
	3676031	70 35	1001	36	Examples X05344	X05344	Human mkny for camerant D
77 CATGGAAATACAGTT	H27/170						

· () = · · · · -

				Ī	1,411923	Human cathengin D mRNA, complete cds
					CCALIMI	Litatus et Homo saniens cDNA clone 110909 3' similar to SP.R151.9
	A 000000	7	5 14	26	Exemples T90296	CE00827
'N CATGGAAATGATGAG]	(AA320942	BST23523 Adipose tissue, brown Homo sapiens cDNA 3' end
			+			zp64f07.s1 Stratagene endothelial cell 937223 Homo sapiens curry close
or contabacations	H533436 3	7	16 6	28	Examples AA181811	624997 3' JOSEPH SORTES DEGRANT UTERUS NDEEPU Homo sapiens CDNA clone
				40	AA148508	491530 3 similar to WP:ZK652.2 CE00448
A CT COTTON	H540621 6	3	6 01	28	Examples L21950	Human peripheral benzodiazepine receptor related involved
SO CATGGAATTIANA	L				M36035	Human penpileral neuromazopino vecepra (1-1-1)
	H540673	77	10	17	No Match	(MEAD)
CATGGACAAAAAA	H545152 0		=	2	Examples U19718	Hunan microhbril-associated Erycomoduli (Mr. 27)
CATGGACCACCTTA	0 0585851	F	0; 20	18	Examples M75165	H.sapiens epitucital tropomy using the sapiens epitucian mp.N.A
CATGGACCAGGCCCT	1	1	<u> </u>		M12125	Human fibroblast muscie-type nepolity bank market
		1	-		M74817	Human tropomyosin-1 (1M-beta) muday, compress cas
			71	15	Examples M74092	Human cyclin mRNA
NA CATGGACCCCAAGGC	H546059 2	7	\perp	\perp	Examples L37033	Homo sapions FK-506 binding protein hamologue
SA CATGGACCCTGCCCT	H546710 3	2	1			2b37g02.s1 Soares parathyroid tumor NoHPA Homo sapiens culva cione
	09080911		0 13		Examples N90046	305810 3'
AN CATSGACCTATCTCT			L			[z]06a10.s] Soares pregnant uteius tvoru o monto agracia
					AA115048	
		7	5 32	[Examples M63193	Human platelet-derived endothelial cell growni lacua
NT CATGGACGGCGCAGG	1				<u> </u>	Human gamma-tubulin mRNA,
NA CATGGACTCTCTGTT	-	10				Human mRNA (HA1753) for ORF
NU CATGGAGAGCTTTGC	1	1	ľ		Examples	TIMP-1=metalloproteinass inhibitor
AU CATGGAGAGTGTCTG	oconocH				L	EPA glycoprotein (erythroid-potentiating activity)
		1	+		X03124	tissue inhibitor of metalloproteinase 2
	11561807	0	-	1 12	No Match	
1 CATGGAGCAGGATGA	11001001		-			Special of Source NhHTGBC Home senions cDNA clone 682848 3'
92 CATGGAGGGAGTTCC	H567486		-	4 13	Examples AA414543	T
		\perp	,	10	Examples	H. sapiens mRNA for neurotensin receptor.
1) CATGGAGTCCGGAGC	H570/8/	5 6	7 -	01		yr27a10.s1 Homo sapiens cDNA clonc 206490 3
94 CATGGAGTTATGTTG	loco7/CH		,]		

					, M	W94333	ze12c08.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 358766 3' similar to SW:YA94_SCHPO Q09783 HYPOTHETICAL 11.4 KD PROTBIN C13G6.04 IN CHROMOSOME 1
TO A COMMON TO A PROPERTY OF A	H572806	7 3	7 15	29	No Match		. S.
95 CATGGAGTTCGACCT			.	5	7		zK/Zdű6,si Soares pregnant utatus trom Carama Carama A88363 3
V6 CATGGATTAAGTGAG	H585913	3	2 2	2	S S S S S S S S S S S S S S S S S S S		yq06g03.s1 Homo sapiens cDNA clone 196180 3'
			-				zk46c12.51 Soares pregnant uterus NoHPU fromo sapicius COM cione
	G			1	A.	36	4838/8 3
OFCATTGAACCTC	H587800	1 0	1	2	Examples Uouzuo		וונכחון) ז פוכנסי מעשבים ליי
98 CATGGCAAAAAAA	H589825		25 2	8 2	No Match		Human mRNA for clongation factor-I-beta.
99 CATGGCATTTAAATA	H605956	2	0	1	X		H. sapiens mRNA for clongation factor 1-beta
		<u> </u>		-	Evamples [10802]		Human nicotinamide N-methyltransferase (NNMT) mRNA, 0
100 CATGGCCAACAAGGA	H606471	5 F	2 5	10	Examples X15256		Human mRNA for 14kDa beta-galactoside-binding lectun
101 CATGGCCCCCAATAA	HOLLON				×		Human mRNA for beta-galactoside-binding lectin
					DI N		Human 14 kd Jecun muter, Wangin
					S4	244881	HL14=beta-galactosido onimis process
							zk82d04.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone
LEGUL	H616224	0	3	16	Examples AA054483	A054483	489319 5' similar to contains Alu rependye element.
102 CATGGCCGCIACLIC							similar to go:X02492 INTERFERON-INDUCED PROTEIN 6-16
	H617891	8	2 44	m	Examples AA243725	A243725	PRECURSOR (HUMAN)
103 CATGGCCG1CGAGG	H618841		4 23	39	Examples X13425	13425	Human mknA 101 paneteant exercises NoHPU Homo sapiens cDNA clone
	772FE3H	3	5 27	9	Examples AA136985	A136985	491117 3'
105 CATGGCGGGGTGGAG							2170h04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 510007
などとしているというというという	H643707	12 29	24 35		Examples AA053346	A053346	3' similar to gb:Z21507 BLONGATION FACTOR 1-DELLA
101 CATGGCTTTTCAGAC	H655177	1 6	7 13	2	Examples 045306	1152819	Human vascular endothelial growth factor B 186
	100000	8	30 16	38	Examples M38259	438259	Human cytochrome c oxidase subunit VIb
108 CATGGGAAAAAAA	H635301				-	M60748	Human histone H1 (H1F4) gene, complete eds

Human (clone SF1) hepatocyte growth factor (HGF) Human (clone SF2) hepatacyte growth factor (HGF) Human mRNA for alpha 1-antitrypsin carboxyterminal, 0 Human mRNA for alpha 1-antitrypsin Human messenger RNA for alpha-1-antitrypsin Human alpha-1 antitrypsin gene, 3' end	zi22b01.s1 Soares pregnant uterus NbHPU Homo sapiers 502633 3' zd86f06.s1 Soares fetal treart NbHH19W Homo sapiens 347555 3' vo72h08.s1 Homo sapiens cDNA clone 183519 3'	Human mRNA for proteasome subunit HsC10-II. , 0 za78c01.s1 Homo sapiens cDNA clone 298656 3' yt92e01.s1 Homo sapiens cDNA clone 231768 3'	seq2272 Homo sapiens cDNA clone ssb4HB3MA(extended-ft-6) 3' H. sapiens RNA for snRNP protein B Human small nuclear ribonucleoprotein particle SmB	Human insulin-like growth factor binding protein 6 Human insulin-like growth factor binding protein 6 za78408.s1 Homo sapiens cDNA clone 178311 3' yo18108.s1 Homo sapiens cDNA clone 178311 3'		35
H655547 18 13 3 70 1 Examples X02920 X01683 X01683 X01683 X01683	H658059 0 0 4 6 16 Examples AA127040 W81387	H666943 6 5 6 10 32 Examples D26598 H667367 0 0 1 1 10 Examples N74310 H92750	H671455 3 7 13 5 21 Examples X17567	H677330 0 0 2 9 22 Examples M69034 M62402 M677753 0 1 4 7 14 Examples N74323 H46766	H686815 0 1 3 13 22 Examples AA074777 AA062735	H688713 25 7 9 0 72 No Match H690863 2 3 1 16 2 No Match H693112 1 1 3 39 2 Examples V00523 H693112 1 1 3 39 2 Examples V00523 K00171
III) CATGGGAAAAGTGGT	110 CATGGGAAGGGAGGC	III CATGGGAGTCATTGT	113 CATGGGATTGTCTGG	114 CATGGGCCCTCACC	116 CATGGGCTGGTCTGG	117 CATGGGGAAGCAGAT 118 CATGGGGAGGGTGG 119 CATGGGGAGGTAGCA 120 CATGGGGCATCTCTT

							1.1. July Lane chair gans 2 Pank
							numen nix-ut nixay y want bours, and pully
	1 10401	101	2	4.	Examples U18009		Human chromosome 1/4/1 mixiva ciono en 113.
21 CATGGGTGGGGAGAT	H / 13401		1	-	<u> </u>		BST57778 Homo sapiens cDNA 3' end similar to Notic
			-	+		N.	EST57474 Homo sapiens cDNA 3' end similar to None
			14-	30	Pxamples M59911		Human integrin alpha-3 chain mRNA
12 CATGGTACTGTAGCA		7 5	2 2	3 5	Ryamoles X87689		H. sapiens mRNA for putative p64 CLCP protein
23 CATGGTACTGTGGCT	١,	2 9	2 0	<u> </u>	Ryamules 1, 12350		Human thrombospondin 2 (THBS2) mRNA
14 CATGGTCAAAATTC		7 20 0	2 12	1 2	Examples D21261		Human mRNA (HA1756) for ORF
125 CATGGTCTGGGGCTT	C7 96775/H	1	2	-			Human keratinocyte cDNA, clone 686
	\perp	1000	12	-	Examples H51290		yp07a05.91 Homo sapiens cDNA clone 186704 3
116 CATGGTCTGTGAGAG	17575/H	╬	1	1			yx44g12.81 Homo sapiens cDNA clone 264646 3
			+	+			2076c09.s1 Stratagene panereas (#937208) Homo sapiens contra crone
						AA158271	592840 3'
	17762631	0	-	13	No Match		
27 CATGGTCTGTGCAGG	1	1	-	19	No Match		
28 CATGGTCTTGAAGCC	4	1	-	00	Evamules X87373		Class C, H.sapiens RPS3a gene
29 CATGGTGAAGGCAGT		*	= -	3 5	Evenuales X08058		GLUTATHIONE S-TRANSFERASE P (HUMAN)
CATGGTGAATGACGG	\perp		1	2 2	Denmiles X51439		Human mRNA for serum amyloid A (SAA) protein
31 CATGGTGCGGAGGAC	_1		=	7	To the second		Human SuRNP core protein Sm D2 mRNA
22 CATCGTGCTGGAGAA	H761481	2 9 9	=	2	Examples Oraco	T	Catatin M (CST6)
ST CHTCGTGGAGGGCAC	H762533			- 1	Examples 002000	COZOGO	1212112 81 Home septens cDNA clone 177767 31
11 CATEGORGEACAGGA	H765003 1	14 17 15	39		Examples	DC+O+U	Al 3206.81 Soares fetal heart NbHH19W Homo sapiens cDNA clone
						AA047563	376786 31
			1	+			zol3f02.si Stratagene colon (#937204) Homo sapiens Const Cloure Section
						AA130701	34
	H774620	0 2 1	13	3	Examples X59288	X59288	H. capiens gene for intercential authority and the
13 CATGGTTCACTGCAG	TI CHOEN		_	-		M24283	Human major group thindvirus receptor (tax v) magaza
		-				103132	Human intercellular adhesion molecule-1 (10-10-1)
		-		-		M55100	Human cell surface glycoprotein P3.38 intura
	H781873	1 1 6	98	24	Examples K02765	K02765	Human complement component C3 mkNAA, aiplia and occa
1 to CATGGTTGTCTTTG		178 110 14	340	139	Examples M17987	MI7987	Human beta-2-microgrounni gene
17 CAT GGT TET GGT I AA	H782391	1 6 12	4	14	Examples D00760	D00760	Human michael of the second and the second second and the second
CALGOLLIAN CAL		-		2	Examples X57025	X57025	INSULIN-LIKE GROWTH FACTOR IA PRECURSOR (HUMAN)
13 CATGTAAGGCTTAAC	H797169	5 6	7 0	1 =	No Match		
CATGTAATTTTGGAA	H802793	_	_]_				

Zk05h07.81 Soares pregnant uterus NbHPU Homo sapiens cDNA clone	99	Examples AA169614 GELATINASB-ASSOCIATED LIPOCALIN PRECURSOR GELATINASB-ASSOCIATED LIPOCALIN PRECURSOR 2b15408.51 Homo sapiens cDNA clone 302127 3' similar to		zm90h04.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 545239 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL Ryamnles AA075896 GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR		Franciles AA100279 3			Examples AA029262 470088 3' Soares fetal liver spleen INFLS Homo sapiens cDNA clone yy66e10.s1 Soares fetal liver spleen INFLS Homo sapiens cDNA clone	N54281 247722 3'	AA114075 cDNA clone 564098 3'	П				Examples L35240 Human emgras gence Example L34 (RPL34) mRNA		Examples X03473 Human gene to transmit attack. NbHPU Homo sapiens cDNA clone 2k23g08.51 Scares pregnant uterus NbHPU Homo sapiens cDNA clone	Examples AA034505 471422 3'
	Examples AA0278 Examples M25753 T60151 R67969		Examples N79823										4 Example				50 Example	15 Example	1 Example
	12	43	19	6		1,2			16			48		27					
	11 2	13	11		7		7 17	1_	4			7 22	L	1	-	3 22	26 18	16 25	1 21
-	3 8	13 3	9		31		m v		9		-	15		1_		m	21	7	
+	0-	-	<u>w</u>	1	2		0	+	77		-	=======================================	10	7=		m	æ	ত	0
	H932731 H938876	H939841	H939849		H939851 H920392		H941856	F1944038	H949560			19023351	10252773	A8002001	11307061	H975446	H976644	H978687	H997944
	158 CATGTGATGTCTGGT 159 CATGTGCCATCTGTA	IKO CATGTGCCCTCAAAA	Adda	[6] CATGTGCCCT CAGA	162 CATGTGCCCTCAGGA	107 CATETECCTCACC	163 CATGTGCCTTACTTT	Ind CATGTGCGCTGGCCC	105 CATGIGCTICATCIG				Ind CATGTGGAGTGGAGG	167 CATGTGGCCCCAGGT	ION CATGTGGGTGAGCCA	E C C C C C C C C C C C C C C C C C C C	169 CATGTGTGAGCCCCI	170 CATGTGTGTGTTTGT	1"2 CATGITATGGATCTC

П	Human lymphocyte cannot the state growth factor	1	y178c08.s1 Homo rapiens cDNA clone 44273 3'	EST94173 Homo sapiens cDNA 3' end similar to None	AA253218 zr53g10.s1 Soares NhHMPu S1 Homo sapiciis Lora contra	
Examples	M20472	Examples X78947	H06492	T35952	AA25321	
0 6 3 7 17		0 16 1				
9 0 96680011	1	H1041504 2 0		H1044225		
1.0	NI CATGITICCTICCIT	CATCATTGCACCTTT		IN CATGITIGITAAAA		

Table 5 - Transcripts increased in pancreas and colorectal cancer

SAGE tag that were elevated in both in coloreactal and pancreatic fumor, and are likely to be specific for tumor in general.

			Description
Company	-	Tag Number Accession	
		- 0401M10629	5
1 CATG TGGAAATGAC C	1	STECKET OF FOCE	Himan retinoic acid induced RIG-E precursor (E) mR
CATG CACTTCAAGG G		016240 061462-	Himman thimic shared antigen-1/stem cell antigen-2
		056145	Compaction many complete cds.
3 CATG ATGTGAAGAG T	T(A)	-243747 303040	Human SPARL/Osteonectan
		M25746	Human osteonectin gene exemply (filamin) (AB
Chara GCCCAAGGAC C		-610466X53416	
T DATESTANCE OF		-229106 X02761	Human mRNA for Ilbronectin (fin precessor)
		K00799	coding region and
O SABURGERON OF ACT		-760291 X58536	Human mRNA for HLA Class I locus C neavy Commission
	T	M26432	gene, comprete
CATC ACAGGCTACG G		-76231 M95787	מ לובות (בוובן
		M83106	Human SM22 mRNA, 3 enu.
A TRUTTOTOTO DE LA		-769020 M77349	Human transforming growth ractor beta induced general
		-589267 X53279	Human mRNA for placental-like alkaline process
		X55358	H. sapiens mRNA for alkaline phosphacese.
		304948	of the second
		-85882 X57351	Ruman 1-8D gene from interferon-inducible gene Lam
10 CATG ACCATTCTGC		1x02490	Human interferon-inducible mRNA (cDNA 1-8).
		- SB04 X15804	Human mRNA for alpha-actinin.
		0.00000 10001.0	Himan mRNA for KIAA0190 protein.
1	C, T	7700077778575-	uman TR2 dene mRNA, 3' end.
13 CATG ATGTAAAAA T		-241665M/4090	
		TARCOL	1
		M19045	Human lysozyme month compression involved in developme
14 CATG GGCAGAGGAC C		-673954 X17620	1
		X75598	R. sapiens nuclar yene.
15 CATG AATATTGAGA A	,	-53129 062962	Human Int-b make, comprete cas:
16 CATG TTTTTGATAR A	-	-1048113 D16891	Human nepek 3 region cannot be fibrilla-1 C.
	7	-302741 X53743	H.saptens minn tot the transfer of the saptens

c		C KEEK.	_	7 5 0 0 V T 0 5 5 7 7 1		
기 2	18 CATG GTTCACATIA	1	1		M13560	Human Ia-associated invariant gamma-chain gene, ex
\dashv			1	-2056	-2056 Y00345	mRNA for polyA binding protein.
19 CATG	ATG AAAAGAAACI		1	-58533	58533M61831	(AHCY)
20 C	20 CATG AATGCAGGCA	SGCA G	+		M61832	Human S-adenosylhomocysteine hydrolase (AHCY) mRNA
\dashv			-	-918273 X16934	X16934	1
21 21	CATG TGAAAIAAAA		+		M28699	Homo sapiens nucleolar phosphoprotein BZ3 (NFM1) m
\dashv					M23613	
\dashv			+		M26697	Human nucleolar protein (B23) mRNA, complete cds.
		E 74.60	-	-998030 M24194	M24194	Human MHC protein homologous to chicken B complex
22 C	CATG TIMIGGGALC	שיייייי ד		-274492 D23661	023661	6
計	23 CATE CARLAR	10100	-		111567	- 8
+		a a a a a a a a a a a a a a a a a a a	-	-155632 083174	D83174	Human mRNA for collagen binding protein 2.
2 7 2	24 CATG AGCCITIBIL	1611	+	-9707B	-97078 X57352	., 1
25 C	25 CATG ACCIGIATCC	ATCC	+	20,000	117006	Himan acidic ribosomal phosphoprotein Pl mRNA, com
26C	CATG TTCAATAAAA	AAAA A		-1000133 MT/800	000/TW	Luna transcobalamin I mRNA, complete cds.
\dagger					20200	1
27.0	CATG CGACCCCACG	CACG C		-398663 M12529	M12529	aportportein E (ensi)
-					K00396	applipoprocess a termination ubiquitie
28.6	CATG CAGATCTTTG	TTTTC		-298495 X56998	X56998	
:					x56999	Human UDA32 praceficat managed fic hypomethy
296	29 CATG CTGGCGAGCG	3AGCG C		-501287	501287 X07491	Human DNA inserts shorting For
+					M91670	Human upiquiting cartes group 1-7.
100	TO CATE ATTERCTIAN	CTTAR A	_	-256497	-256497 L14272	ı
3	2112				885655	prohibitin inuman, man, 1942
15	CATC GTGGACA	GGACA		-765573	-765573 062435	Human nicotinic acetylciotine receptor
1					068041	Calicer subscription
1	Chara areases	CCCCA		-883025	-883029 M24398	
77	DULUK OFAC	T	-	-125661		H. sapiens RNA IOr nmc3-nc yene.
7	מאום שרזה				M36981	train were
1			+		L16785	actor
				-33331	1 002032	partian
34	CATG AAGAM	AAGAAGATAG	+		0137230	сошртеге

T	ACTUTION	ressed pro
T	T79083 L0830 Human homology	Human ribosomal protein 112 mRNA, complet
T	T -507577 D14530 Human nomonous X57959 H.saplens mR X57959 H.saplens mR X57959 H.saplens mR X57959 H.saplens mR X57959 Human riboso L16559 Human riboso L16559 Human riboso Saplens A -672265 L19527 Homo saplens MR X13710 Human gene f X13710 Human gene f X13710 Human gene f X13709 Human gene f MR1304 Human glutat MR1304 Human liver C -507455 X04347 Human liver C -507455 X04347 Human liver C -507455 X04347 Human mRNA -239533 X17206 Human mRNA D17652 Human mRNA S76343 AMD1EAP S76343 Human mRNA S76343 Human mRNA S76343 Human mRNA S76343 Human mRNA X03569 Human mRNA X03569 Human HepG2 D17182 Human HepG2 D17276 Human HepG2 D17276 Human HepG3 D172776 Human HepG3 D17276 Human	numming of yeart ribosomal protein 528,
T	T	
X57956 H. saplens mRNA for ribosomal protein 17.	ATTAITILE	H. saplens mRNA for ribosomal process
X52967 Human mRNA for Tibosomal protein L7 (RPL7) mRNA, complete L16566 Human tibosomal protein L7 (RPL7) mRNA, complete L1655115 106499 Human at thosomal protein L7 (RPL7) mRNA, complete L5216 GCCTTTAAGG A	A	H. sapiens mRNA for ribosomal protein
CATG GCCAAGAAGA	116558 Human riboso	Human mRNA for ribosomal protein L/
CATG GCTTTTAAGG	CATG GCTTTTAAGG A -655115 L06498 Homo saptens CATG GCCAAGAAGA A -67265 L19527 Homo saptens CATG CTCTTCGAGA A -490889 Y00433 Human nRNA f X13710 H.sapiens un X13710 H.sapiens un X13710 H.man gene f X13710 H.man gene f X13709 Human glutat MZ1304 Human glutat MZ1304 Human clone CATG CTGGTTAAT A -507455 X04347 Human clone CATG GATGCTGCCA A -583573 X17206 Human mRNA CATG GATGCTGCCA A -583573 X59357 Human mRNA CATG CTCTCGAGAT C -583573 X59357 Human mRNA CATG CTCTCGAGAT C -482584 U16811 Human BAK m CATG TGTTGAGA G -978825 X16869 Human mRNA CATG TGTTTGAG G -978825 X16869 Human mRNA X03558 Human mRNA X03559 Human mRNA	Human ribosomal protein L7 (RPL7) mRNA, complete
CATG GCCAAGAAGA	CATG GCTTTTAAGG A -672265 L19527 Homo saptens CATG GCCAAGAAGA A -490889 Y00433 Human nRNA f CATG CTCTTCGAGA A -490889 Y00433 Human gene f X13710 Human gene f M21304 Human gene f M21304 Human nRNA c CATG CTGGGTTAAT A -507455 X04347 Human nRNA c CATG GATGCTGCCA A -503533 X17206 Human mRNA c CATG GATGCTGCCA A -583573 X59357 Human mRNA c CATG GATGCTGCCA A -583573 X59357 Human mRNA c CATG GATGCTGCCA A -583573 X59357 Human mRNA c CATG CTCTCGAGAT C -390692 U14970 Human mRNA c CATG GTGTTGAGA G -978825 X16869 Human mRNA x03569 Human HepGZ D1726 Human HepGZ D17276 Human HepGZ D1726 Human HepGZ D17276 Human HepGZ D1	106498 Homo sapiens ribosomal protein S20 (RFS20) makes,
CATC CTCTCGAGA	CATG GGCAAGAAGA A — 490889 Y00433 Human nENA for	1.19527 Homo sapiens ribosomal protein L27 (RFLZ7) mmnn,
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114 CATG GCCTCTGCC A	-613862	100 H
115 CATG AACAGAAGCA A	-18469	EUA.
116 CATG CTGCCGAGCT C	-497192	Toda
117 CATG TICCTCGGGC A	-1007018	100 P
118 CATG AACTAATACT A	-28872	7 E 22 E
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Isolation of partial cDNA (3' fragment) by 3' directed PCR reaction

This procedure is a modification of the protocol described in Polyak et al. (1997) Nature 389:300. Briefly, the procedure uses SAGE tags in PCR reaction such that the resultant PCR product contains the SAGE tag of interest as well as additional cDNA, the length of which is defined by the position of the tag with respect to the 3' end of the cDNA. The cDNA product derived from such a transcript driven PCR reaction can be used for many applications.

RNA from a source believed to express the cDNA corresponding to a given tag is first converted to double-stranded cDNA using any standard cDNA protocol. Similar conditions used to generate cDNA for SAGE library construction can be employed except that a modified oligo-dT primer is used to dreive the first strand synthesis. For example, the oligonucleotide of composition 5'-B-TCC GGC GCG CCG TTT T CC CAG TCA CGA(30)-3', contains a poly-T stretch at the 3' end for hybridization and priming from poly-A tails, an M13 priming site for use in subsequent PCR steps, a 5' Biotin label (B) for capture to strepavidin-coated magnetic beads, and an AscI restriction endonuclease site for releasing the cDNA from the streptavidin-coated magnetic beads. Theoretically, any sufficiently-sized DNA region capable of hybridizing to a PCR primer can be used as well as any other 8 base pair recognizing endonuclease.

cDNA constructed utilizing this or similar modified oligo-dT primer is then processed exactly as described in U.S. Patent No. (insert) up until adapter ligation where only one adapter is ligated to the cDNA pool. After adapter ligation, the cDNA is released from the streptavidin-coated magnetic beads and is then used as a template for cDNA amplification.

Various PCR protocols can be employed using PCR priming sites within the 3' modified oligo-dT primer and the SAGE tag. The SAGE tag-derived PCR primer employed can be of varying length dictated by 5' extension of the tag into the adaptor sequence. cDNA products are now available for a variety of applications.

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This technique can be further modified by: (1) altering the length and/or content of the modified oligo-dT primer; (2) ligating adaptors other than that previously employed within the SAGE protocol; (3) performing PCR from template retained on the streptavidin-coated magnetic beads; and (4) priming first strand cDNA synthesis with non-oligo-dT based primers.

Isolation of cDNA using GeneTrapper or modified GeneTrapper Technology

The reagents and manufacturer's instructions for this technology are commercially available from Life Technologies, Inc., Gaithersburg, Maryland. Briefly, a complex population of single-stranded phagemid DNA containing directional cDNA inserts is enriched for the target sequence by hybridization in solution to a biotinylated oligonucleotide probe complementary to the target sequence. The hybrids are captured on streptavidin-coated paramagnetic beads. A magnet retrieves the paramagnetic beads from the solution, leaving nonhybridized single-stranded DNAs behind. Subsequently, the captured single-stranded DNA target is released from the biotinylated oligonucleotide. After release, the cDNA clone is further enriched by using a nonbiotinylated target oligonucleotide to specifically prime conversion of the single-stranded target to double-stranded DNA. Following transformation and plating, typically 20% to 100% of the colonies represent the cDNA clone of interest. To identify the desired cDNA clone, the colonies may be screened by colony hybridization using the 32P-labeled oligonucleotide as described above for solution hybridization, or alternatively by DNA sequencing and alignment of all sequences obtained from numerous clones to determine a consensus sequence.

The genes which are identified herein as being differentially expressed in normal and cancer cells can be used diagnostically and prognostically. Transcription levels in a test sample suspected of being neoplastic can be determined and compared to the levels in normal colon cells. The test sample may be from any tissue suspected of neoplasia, and particularly from either suspected colorectal or suspected pancreatic cancer cells. The control cells for

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the purposes of comparison are normal cells, preferably of the same tissue type as the test sample, e.g., colon cells, or pancreatic duct epithelial cells. Upregulation of transcription or downregulation of transcription is therefore diagnostic of the neoplastic state, depending on what gene is used as a test reagent. Similarly, transcription levels can be monitored to assess patent responses to anti-tumor therapies. Transcription levels will also provide prognostic information. For example, the level of transcription in a test sample can be compared to levels found in bona fide normal and tumor cells. More extreme deviations from normal expression levels indicate a poorer prognosis.

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Transcription levels can be determined according to any means known in the art. These include, without limitation, Northern blots, nuclear run-on assays, in vitro transcription assays, primer extension assays, quantitative reverse transcriptase-polymerase chain reactions (RT-PCR), and hybrid filter binding assays. These techniques are well known in the art. See J.C. Alwine, D.J. Kemp, G.R. Stark, *Proc. Natl. Acad. Sci. U.S.A.* 74, 5350 (1977); K. Zinn, D. Di-Maio, T. Maniatis, *Cell* 34, 865 (1983); G. Veres, R.A. Gibbbs, S.E. Scherer, C.T. Caskey, *Science* 237, 415 (1987).

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Similarly, upregulated genes and downregulated genes can be detected by measuring expression of their protein products. This can be done by any means known in the art, including but not limited to Western (immuno) blot, enzyme linked immunoadsorbent assay, radioimmunoassay, and enzyme assay. Such techniques are well known in the art. Protein products can be detected in tissue samples of a test patient, using a suspect sample as a test sample, and a matched normal tissue sample from the same tissue type as a control. If normal tissue is not available then a closely related tissue type can be used. Desirably both the samples being compared will be from the same individual. Alternatively, aberrant expression levels of protein products can be detected in body samples, such as blood, serum, feces, urine, sputum. As a control, a normal matched sample can be used from a healthy individual. Aberrant expression levels of transcripts can also be detected in such body samples, particularly in blood and serum.

Probes for use in the assays for transcription levels of particular genes or sets of genes may be RNA or DNA. The probes will be isolated substantially free of other cellular RNAs or DNAs. If the reagent contains one probe then it will comprise at least 50% of the nucleic acids in the reagent composition. If the reagent contains more than one probe, then the proportion will decrease accordingly, so that specific probes will still comprise at least 50% of the nucleic acids in the reagent composition.

Probes can be labeled according to any means known in the art. These may include radioactive labels, fluorescent labels, enzymatic labels, and binding partner labels such as biotin. Means for labeling and detecting probes are well known in the art. Probes comprise at least 10, 11, 12, 15, 20, or 30 contiguous nucleotides of a selected gene.

This invention provides proteins or polypeptides expressed from the polynucleotides of this invention, which is intended to include wild-type and recombinantly produced polypeptides and proteins from procaryotic and eucaryotic host cells, as well as muteins, analogs and fragments thereof. In some embodiments, the term also includes antibodies and anti-idiotypic antibodies.

It is understood that functional equivalents or variants of the wild-type polypeptide or protein also are within the scope of this invention, for example, those having conservative amino acid substitutions. Other analogs include fusion proteins comprising a protein or polypeptide.

The proteins and polypeptides of this invention are obtainable by a number of processes well known to those of skill in the art, which include purification, chemical synthesis and recombinant methods. Full length proteins can be purified from a colon or pancreatic cell or tissue lysate by methods such as immunoprecipitation with antibody, and standard techniques such as gel filtration, ion-exchange, reversed-phase, and affinity chromatography using a fusion protein as shown herein. For such methodology, see for example Deutscher et al. (1999) Guide To Protein Purification: Methods In Enzymology (Vol. 182, Academic Press). Accordingly, this invention also

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provides the processes for obtaining these proteins and polypeptides as well as the products obtainable and obtained by these processes.

The proteins and polypeptides also can be obtained by chemical synthesis using a commercially available automated peptide synthesizer such as those manufactured by Perkin Elmer/Applied Biosystems, Inc., Model 430A or 431A, Foster City. The synthesized protein or polypeptide can be precipitated and further purified, for example by high performance liquid chromatography (HPLC). Accordingly, this invention also provides a process for chemically synthesizing the proteins of this invention by providing the sequence of the protein and reagents, such as amino acids and enzymes and linking together the amino acids in the proper orientation and linear sequence.

Alternatively, the proteins and polypeptides can be obtained by well-known recombinant methods as described, for example, in Sambrook et al., (1989), supra, using the host cell and vector systems described above.

Also provided by this application are the polypeptides and proteins described herein conjugated to a detectable agent for use in the diagnostic methods. For example, detectably labeled proteins and polypeptides can be bound to a column and used for the detection and purification of antibodies. They also are useful as immunogens for the production of antibodies as described below. The proteins and fragments of this invention are useful in an in vitro assay system to screen for agents or drugs, which modulate cellular processes.

The proteins of this invention also can be combined with various liquid phase carriers, such as sterile or aqueous solutions, pharmaceutically acceptable carriers, suspensions and emulsions. Examples of non-aqueous solvents include propyl ethylene glycol, polyethylene glycol and vegetable oils. When used to prepare antibodies, the carriers also can include an adjuvant that is useful to non-specifically augment a specific immune response. A skilled artisan can easily determine whether an adjuvant is required and select one. However, for the purpose of illustration only, suitable adjuvants include, but

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are not limited to Freund's Complete and Incomplete, mineral salts and polynucleotides.

This invention also provides a pharmaceutical composition comprising any of a protein, analog, mutein, polypeptide fragment, antibody, antibody fragment or anti-idiotipic antibody of this invention, alone or in combination with each other or other agents, and an acceptable carrier. These compositions are useful for various diagnostic and therapeutic methods.

Antibodies can be generated using the proteins encoded by the transcripts identified by the tags disclosed herein. Use of all or portions of the protein as immunogens is routine in the art. Similarly, fusion proteins can be used as immunogens. Antibodies can be affinity purified using the proteins or portions thereof used as immunogens. Similarly, monoclonal antibodies specifically immunoreactive with the protein sequences of the invention can be generated according to techniques which are well known in the art.

Antibodies can be used analytically to quantitate the expression of particular transcripts identified herein as upregulated or downregulated in cancer. In addition, antibodies can be conjugated or non-covalently linked to cytotoxic agents, such as cytotoxins, radionuclides, chemotherapeutic drugs, etc. Such antibodies can be used therapeutically to specifically target cancer cells in which the protein antigens are upregulated. These include the proteins encoded by the transcripts identified by the tags shown in Tables 2, 4, and 5. Means of making such linked cytotoxic antibodies and of administering the same are well known in the art.

Also provided by this invention is an antibody capable of specifically forming a complex with the proteins or polypeptides as described above. The term "antibody" includes polyclonal antibodies and monoclonal antibodies. The antibodies include, but are not limited to mouse, rat, and rabbit or human antibodies.

Laboratory methods for producing polyclonal antibodies and monoclonal antibodies, as well as deducing their corresponding nucleic acid sequences, are known in the art, see Harlow and Lane (1988) supra and

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Sambrook et al. (1989) supra. The monoclonal antibodies of this invention can be biologically produced by introducing protein or a fragment thereof into an animal, e.g., a mouse or a rabbit. The antibody producing cells in the animal are isolated and fused with myeloma cells or heteromyeloma cells to produce hybrid cells or hybridomas. Accordingly, the hybridoma cells producing the monoclonal antibodies of this invention also are provided.

Thus, using the protein or fragment thereof, and well known methods, one of skill in the art can produce and screen the hybridoma cells and antibodies of this invention for antibodies having the ability to bind the proteins or polypeptides.

If a monoclonal antibody being tested binds with the protein or polypeptide, then the antibody being tested and the antibodies provided by the hybridomas of this invention are equivalent. It also is possible to determine without undue experimentation, whether an antibody has the same specificity as the monoclonal antibody of this invention by determining whether the antibody being tested prevents a monoclonal antibody of this invention from binding the protein or polypeptide with which the monoclonal antibody is normally reactive. If the antibody being tested competes with the monoclonal antibody of the invention as shown by a decrease in binding by the monoclonal antibody of this invention, then it is likely that the two antibodies bind to the same or a closely related epitope. Alternatively, one can pre-incubate the monoclonal antibody of this invention with a protein with which it is normally reactive, and determine if the monoclonal antibody being tested is inhibited in its ability to bind the antigen. If the monoclonal antibody being tested is inhibited then, in all likelihood, it has the same, or a closely related, epitopic specificity as the monoclonal antibody of this invention.

The term "antibody" also is intended to include antibodies of all isotypes. Particular isotypes of a monoclonal antibody can be prepared either directly by selecting from the initial fusion, or prepared secondarily, from a parental hybridoma secreting a monoclonal antibody of different isotype by using the sib selection technique to isolate class switch variants using the

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procedure described in Steplewski et al. (1985) Proc. Natl. Acad. Sci. 82:8653 or Spira et al. (1984) J. Immunol. Methods 74:307.

This invention also provides biological active fragments of the polyclonal and monoclonal antibodies described above. These "antibody fragments" retain some ability to selectively bind with its antigen or immunogen. Such antibody fragments can include, but are not limited to:

- (1) Fab,
- (2) Fab',
- (3) F(ab')2,
- (4) Fv, and
- (5) SCA

A specific example of "a biologically active antibody fragment" is a CDR region of the antibody. Methods of making these fragments are known in the art, see for example, Harlow and Lane, (1988) supra.

The antibodies of this invention also can be modified to create chimeric antibodies and humanized antibodies (Oi, et al. (1986) BioTechniques 4(3):214). Chimeric antibodies are those in which the various domains of the antibodies' heavy and light chains are coded for by DNA from more than one species.

The isolation of other hybridomas secreting monoclonal antibodies with the specificity of the monoclonal antibodies of the invention can also be accomplished by one of ordinary skill in the art by producing anti-idiotypic antibodies (Herlyn, et al. (1986) Science 232:100). An anti-idiotypic antibody is an antibody which recognizes unique determinants present on the monoclonal antibody produced by the hybridoma of interest.

Idiotypic identity between monoclonal antibodies of two hybridomas demonstrates that the two monoclonal antibodies are the same with respect to their recognition of the same epitopic determinant. Thus, by using antibodies to the epitopic determinants on a monoclonal antibody it is possible to identify other hybridomas expressing monoclonal antibodies of the same epitopic specificity.

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It is also possible to use the anti-idiotype technology to produce monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the mirror image of the epitope bound by the first monoclonal antibody. Thus, in this instance, the anti-idiotypic monoclonal antibody could be used for immunization for production of these antibodies.

As used in this invention, the term "epitope" is meant to include any determinant having specific affinity for the monoclonal antibodies of the invention. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics.

The antibodies of this invention can be linked to a detectable agent or label. There are many different labels and methods of labeling known to those of ordinary skill in the art.

The antibody-label complex is useful to detect the protein or fragments in a sample, using standard immunochemical techniques such as immunohistochemistry as described by Harlow and Lane (1988) supra. Competitive and non-competitive immunoassays in either a direct or indirect format are examples of such assays, e.g., enzyme linked immunoassay (ELISA) radioimmunoassay (RIA) and the sandwich (immunometric) assay. Those of skill in the art will know, or can readily discern, other immunoassay formats without undue experimentation.

The coupling of antibodies to low molecular weight haptens can increase the sensitivity of the assay. The haptens can then be specifically detected by means of a second reaction. For example, it is common to use haptens such as biotin, which reacts avidin, or dinitropherryl, pyridoxal, and fluorescein, which can react with specific anti-hapten antibodies. See Harlow and Lane (1988) supra.

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The monoclonal antibodies of the invention also can be bound to many different carriers. Thus, this invention also provides compositions containing the antibodies and another substance, active or inert. Examples of well-known carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, agaroses and magnetite. The nature of the carrier can be either soluble or insoluble for purposes of the invention. Those skilled in the art will know of other suitable carriers for binding monoclonal antibodies, or will be able to ascertain such, using routine experimentation.

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Compositions containing the antibodies, fragments thereof or cell lines which produce the antibodies, are encompassed by this invention. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

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The present invention also provides a screen for various agents which modulate the expression of a gene in a pancreatic or colon cell. To practice the method in vitro, suitable cell cultures or tissue cultures are first provided. The cell can be a cultured cell or a genetically modified cell in which a trancript from SEQ ID NOS:1-732, or their complements, is expressed. Alternatively, the cells can be from a tissue biopsy. The cells are cultured under conditions (temperature, growth or culture medium and gas (CO₂)) and for an appropriate amount of time to attain exponential proliferation without density dependent constraints. It also is desirable to maintain an additional separate cell culture; one which does not receive the agent being tested as a control.

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As is apparent to one of skill in the art, suitable cells may be cultured in microtiter plates and several agents may be assayed at the same time by noting genotypic changes, phenotypic changes or cell death.

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When the agent is a composition other than a DNA or RNA, the agent may be directly added to the cell culture or added to culture medium for addition. As is apparent to those skilled in the art, an "effective" amount must be added which can be empirically determined. When the agent is a polynucleotide, it may be directly added by use of a gene gun or

electroporation. Alternatively, it may be inserted into the cell using a gene delivery vehicle or vector as described above.

An agent is a potential therapeutic if it alters the expression of gene in the cell. Altered expression can be detected by assaying for altered mRNA expression or protein expression using the probes, primers and antibodies as described herein.

For the purposes of this invention, an "agent" is intended to include, but not be limited to a biological or chemical compound such as a simple or complex organic or inorganic molecule, a peptide, a protein (e.g. antibody) or a polynucleotide (e.g. anti-sense). A vast array of compounds can be synthesized, for example polymers, such as polypeptides and polynucleotides, and synthetic organic compounds based on various core structures, and these are also included in the term "agent". In addition, various natural sources can provide compounds for screening, such as plant or animal extracts, and the like. It should be understood, although not always explicitly stated that the agent is used alone or in combination with another agent, having the same or different biological activity as the agents identified by the inventive screen. The agents and methods also are intended to be combined with other therapies.

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The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following specific examples which are provided herein for purposes of illustration only, and are not intended to limit the scope of the invention.

EXAMPLE 1

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This example demonstrates the characterization of the general transcription of human colorectal epithelium, colorectal cancers, and pancreatic cancers.

We used the recently developed SAGE (serial analysis of gene expression) method to identify and quantify a total of 303,706 transcripts derived from human colorectal (CR) epithelium, CR cancers or pancreatic cancers (Table 1A) (3). These transcripts represented approximately 48,741

different genes (4) that ranged in average expression from 1 copy per cell to as many as 5,300 copies per cell (5). The number of different transcripts observed in each cell population varied from 14,247 to 20,471. The bulk of the mRNA mass (75%) consisted of transcripts expressed at more than five copies per cell on average (Table 1B). In contrast, the majority (86%) of transcripts were expressed at less than 5 copies per cell, but in aggregate this low abundance class represented only 25% of the mRNA mass. This distribution was consistently observed among the different samples analyzed and was consistent with previous studies of RNA abundance classes based on RNA-DNA reassociation kinetics (Rot curves). Monte Carlo simulations revealed that our analyses had a 92% probability of detecting a transcript expressed at an average of three copies per cell (7).

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Table 1 - Summary of SAGE Analysis

A. Overall Summary

	Normal	Colon	Colon	Pancreatic	Pancreatic	
	Colon	Tumors	Cell Lines	Tumors	Cell Lines	Total
Total Tags	62,168	878,09	60,373	61,592	58,695	303,706
Unique Genes¹ GenBank²	14,721 8,753 (59)	19,690 10,490 (53)	17,092 10,193 (60)	20,471 11,547 (56)	14,247 8,922 (63)	48,741 26,339 (54)

¹ Indicates the number of different genes represented by the total tags analyzed (4).

² Indicates the number of genes that matched an entry in GenBank. The number in parentheses indicates the corresponding percentage of total unique tags.

Table 1 - Summary of SAGE Analysis

Normal	Normal	Colon	Colon	Pancreatic	Pancreatic Cell	II.
Copies/Cell	Colon	Tumors	Cell Lines	Tumore	Lines	Total
> 500 Unique Genes	62 (29)	54 (25)	54 (19)	32 (11)	70 (26)	(61) 55
GenBank	(56) 65	52 (96)	53 (98)	32 (100)	70 (100)	54 (98)
> 50 and ≤ 500 Unique Genes	645 (28)	470 (21)	618 (27)	657 (29)	585 (27)	595 (26)
GenBank	545 (84)	429 (91)	579 (94)	(66) 609	529 (90)	553 (93)
> 5 and < 50 Unique Genes	4,569 (27)	5,011 (29)	5,733 (34)	6,146 (36)	4,895 (31)	6,209 (30)
GenBank	2,893 (63)	3,204 (64)	3,682 (64)	4,054 (66)	3,168 (65)	4,241 (68)

41,882 (25)	21,491 (51)
8,697 (16)	5,155 (59)
13,636 (24)	6,852 (50)
10,687 (20)	5,879 (55)
14,155 (25)	6,805 (48)
9,445 (16)	5,256 (56)
≤ 5 Unique Genes	GenBank

the mass fraction (X100) of total transcripts represented by the indicated abundance class. For GenBank entries, the first number indicates the number of different *For unique genes, the first number denotes the number of different genes (4) represented in the indicated abundance class. The number in parentheses indicates genes that matched an entry in GenBank in the indicated abundance class. The number in parentheses indicates the corresponding percentage of total genes. Many of the SAGE tags appeared to represent previously undescribed transcripts, as only 54% of the tags matched entries in GenBank (Table 1). Twenty percent of these matching transcripts corresponded to characterized mRNA sequence entries in GenBank, whereas 80% matched uncharacterized EST entries. As expected, the likelihood of a tag being present in the databases was related to abundance; GenBank matches were identified for 98% of the transcripts expressed at more than 500 copies per cell but for only 51% of the transcripts expressed at \leq 5 copies per cell. Because the SAGE data provide a quantitative assay of transcript abundance, unaffected by differences in cloning or PCR efficiency, these data provide an independent and relatively unbiased estimate of the current completeness of publicly available EST databases.

EXAMPLE 2

This example demonstrates a comparison of the expression pattern of normal colon epithelium and primary colon cancers.

Comparison of expression patterns between normal colon epithelium and primary colon cancers revealed that the majority of transcripts were expressed at similar levels (Fig. 1A). However, the expression profiles also revealed 289 transcripts that were expressed at significantly different levels [P < 0.01, (8)]. Of these 289, 181 were decreased in colon tumors compared to normal colon (average decrease 10-fold; Fig. 1B; examples in Fig. 2A). Conversely, 108 transcripts were expressed at higher levels in the colon cancers than in normal colon (average increase 13-fold; Fig. 1C; examples in Fig. 2A). Monte Carlo simulations indicated that the analysis would have detected over 95% of those transcripts expressed at a 6-fold or greater level in normal vs. tumor cells or vice versa (9). Because relatively stringent criteria were used for defining differences [P < 0.01, (8)], the number of differences reported above is likely to be an underestimate.

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EXAMPLE 3

This example demonstrates the similarities and differences between cancer cell line transcription and transcription of primary cancer tissues. To determine how many of the 289 differences were independent of the cellular microenvironment of cancers *in vivo*, SAGE data from CR cancer cell lines was compared to that from primary CR cancer tissues (Fig. 1B, 1C). Perhaps surprisingly, the majority of transcripts (130 of 181) that were expressed at reduced levels in cancer cells in vivo were also expressed at significantly lower levels in the cell lines (Fig. 1B). Likewise, a significant fraction of the transcripts expressed at increased levels in primary cancers were also expressed at higher levels in the CR cancer cell lines (Fig. 1C). Thus, many of the gene expression differences that distinguish normal from tumor cells in vivo persist during in vitro growth. However, despite these similarities there were also many differences. For example, only 47 of 228 genes expressed at higher levels in CR cancer cell lines were also expressed at high levels in the primary CR cancers.

In combination, comparing the expression pattern of CR cancer cells (in vivo or in vitro) to normal colon revealed 548 differentially expressed transcripts (Fig. 1B,C, Tables 2 and 3). The average difference in expression for these transcripts was 15 fold. Although the ability to detect differences is influenced by the magnitude of the variance with the power to detect smaller differences being less, 92 transcripts that were less than three fold different were identified among the 548 transcripts. However, those genes exhibiting the greatest differences in expression are likely to be the most biologically important.

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EXAMPLE 4

This example demonstrates the similarities and differences between colorectal cancer transcription and pancreatic cancer transcription.

To determine whether the changes noted in CR cancers were neoplasia or cell type specific, we performed SAGE on mRNA derived from pancreatic cancers. A total of 404 transcripts were expressed at higher levels in pancreatic cancers compared to normal colon epithelium (examples in Fig. 2B). The majority (268) of these transcripts were pancreas-specific (10) (Example in Fig. 2C) although 136 were also expressed at high levels in CR cancers. These 136 transcripts constituted 47% of the 289 transcripts increased in CR cancers relative to normal colon and are likely to be related to the neoplastic process rather than to the specific cell type of origin.

EXAMPLE 5

This example demonstrates the reproducibility of the transcription patterns observed among a larger number of cancer samples.

One question that arose from these data is the potential heterogeneity of expression between individual tumors. The SAGE data were acquired from two examples of each tissue type (normal colon, primary CR cancer, CR cancer cell line, etc.). To examine the generality of these expression profiles, we arbitrarily selected 27 differentially expressed transcripts and evaluated them in six to twelve samples of normal colon and primary cancers by Northern blot analysis (11). In general, expression patterns were very reproducible among different samples. Of 10 genes with elevated expression in normal colon relative to CR cancers as determined by SAGE, each was detected in the normal colon samples and was expressed at considerably lower levels in tumors (examples in Fig. 2A). Similarly, most of the genes identified by SAGE as increased in CR or pancreatic cancers were confirmed to be reproducibly expressed in the majority of primary cancers examined by Northern blot (examples in Fig. 2A). It is important to note, however, that there were differences among the cancers, with a few cancers exhibiting particularly high or low levels of individual transcripts. Such differences in gene expression

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undoubtedly contribute to the observed heterogeneity in biological properties of cancers derived from the same organ.

EXAMPLE 6

This example demonstrates the identities of some of the transcripts which were found to be differentially expressed in tumor and normal tissues. What are the identities of the differentially expressed genes? Of the 548 differentially expressed transcripts, 337 were tentatively identified through database comparisons. When tested, the great majority (93%) of these identifications proved to be legitimate (13), as expected from previous SAGE analyses. Although a large number of differentially expressed genes were identified, some simple patterns did emerge. For example, genes that were expressed at higher levels in normal colon epithelium than in CR tumors were often differentiation-related. These genes included liver fatty acid binding protein, cytokeratin 20, carbonic anhydrase, guanylin and uroguanylin, which are known to be important for the normal physiology or architecture of the colon epithelium (Table 2). On the other hand, genes that were increased in CR cancers were often related to the robust growth characteristics that these cells exhibit. For example, gene products associated with protein synthesis, including 48 ribosomal proteins, five elongation factors, and five genes involved in glycolysis were observed to be elevated in both CR and pancreatic cancers compared to normal colon cells. Although the majority of the transcripts could not have been predicted to be differentially expressed in cancers, several have previously been shown to be dysregulated in neoplastic cells. The latter included IGFII, B23 nucleophosmin, the Pi form of glutathione S-transferase, and several ribosomal proteins which were all increased in cancer cells as previously reported. Likewise, Dra and gelsolin were both decreased in cancer as previously reported. Surprisingly, two widely studied oncogenes, c-fos and c-erbb3, were expressed at much higher levels in normal colon epithelium than CR cancers, in contrast to their up-regulation in transformed cells.

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In summary, these data provide basic information necessary for understanding the gene expression differences that underlie cancer phenotypes. They additionally provide a necessary framework for interpreting the significance of individual differentially expressed genes. Although this study demonstrated that a large number of such differences exist (approximately 500 at the depth of analysis employed), it was equally remarkable that the fraction of transcripts exhibiting significant differences was relatively small, representing 1.5 % of the transcripts detected in any given cell type (26). The fact that many, but not all, of the differences were preserved during in vitro culture demonstrates the utility of cultured lines for examination of some aspects of gene expression, but also provides a note of caution in relying on such lines to perfectly mimic tumors in their natural environment. Finally, the finding that hundreds of specific genes are expressed at different levels in CR cancers, and that some of these are also expressed differentially in pancreatic cancers, provides a wealth of new reagents for future biologic and diagnostic experimentation.

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- of tags (30,000) were derived from two different patients for each tissue. For primary tumors (two CR carcinomas and two pancreatic adenocarcinomas), RNA was isolated from portions of tumors judged to contain 60%-90% tumor cells by histopathology. The cells grown in vitro were derived from CR (SW837, Caco2) and pancreatic (ASPC-1, PL45) cancer cell lines. CR epithelial cells were isolated from sections of normal colon mucosa from two patients using EDTA as previously described [S. Nakamura, I. Kino, S. Baba, Gut 34, 1240 (1993)]. Histopathology confirmed that the isolated cells were greater than 90% epithelial. Isolation of Poly-A RNA and SAGE was performed as previously described (2). SAGE data was analyzed by means of SAGE software and GenBank Release 95 as previously described (2).
- 4. A total of 69,393 different SAGE tags were identified among the 303,706 tags analyzed. A small fraction of these different tags were likely due to sequencing errors. SAGE analysis of yeast (2), wherein the entire genomic sequence is known, demonstrated a sequencing error rate of ~ 0.7%, translating to a SAGE tag error rate of 6.8% (1 0.993¹⁰). Because these sequencing mistakes are essentially random, they do not substantially affect the analysis although they could artificially inflate the number of unique genes identified. Therefore, to be conservative, we reduced our estimate of unique genes identified by this maximum tag error rate (e.g., 6.8% of 303,706 total tags). The number of different tags derived from the same gene due to alternative splicing was assumed to be negligible.

- 5. Abundances can be simply determined by dividing the observed number of tags for a given transcript by the total number of tags obtained. An estimate of approximately 300,000 transcripts per cell was used to convert the abundances to copies per cell [N. D. Hastie, J. O. Bishop, Cell 9, 761 (1976)].
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 250, 199 (1974); B. Lewin, Gene Expression Vol 2 (John Wiley and sons,
 New York 1980).
- 7. Computer simulations indicated that analysis of 300,000 tags would yield a 92 % chance of detecting a tag for a transcript whose expression was at least three copies per cell on average among the tissues examined and assuming 300,000 transcripts per cell.
- To minimize the number of assumptions and to account for the 8. large number of comparisons being made, Monte Carlo analysis was used for determining statistical significance. The null hypothesis was that the level, kind, and distribution of transcripts were the same for cancer and normal cells. For each transcript, 100,000 simulations were performed to determine the relative likelihood due to chance alone ("p-chance") of obtaining a difference in expression equal to or greater than the observed difference, given the null hypothesis. This likelihood was converted to an absolute probability value by simulating 40 experiments in which a representative number of transcripts (27,993 transcripts in each experiment) was identified and compared. The distribution of transcripts used for these simulations was derived from the average level of expression observed in the original samples. The distribution of the p-chance scores obtained in the 40 simulated experiments (false positives) was then compared to those obtained experimentally. Based on this comparison, a maximum value of 0.0005 was chosen for p-chance. This yielded a false positive rate that was no higher than 0.01 for the least significant p-chance value below the cutoff.
- 9. Two hundred simulations assuming an abundance of 0.0001 in one sample and 0.0006 in a second sample revealed a significant difference (*P* < 0.01, [8]) 95% of the time.

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- 10. It is not possible to obtain pancreatic ductal epithelium, from which pancreatic carcinomas arise, in sufficient quantities to perform SAGE. It is therefore not possible to determine whether these transcripts were derived from genes that were highly expressed only in pancreatic cancers or were also expressed in pancreatic duct cells.
- 11. Total RNA isolation and Northern blot analysis was performed as described [W. S. el-Deiry, et al., Cell 75, 817 (1993)].
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- 13. Northern blot analyses were done on 45 of the 337 differentially expressed transcripts with tentative database matches. In three cases, the pattern of expression was not differentially expressed as predicted by SAGE and, for the purposes of this calculation, were presumed to represent incorrect database matches.
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 H. Kraus, W. Issing, T. Miki, N. C. Popescu, S. A. Aaronson, Proc Natl Acad Sci USA 86, 9193 (1989).
- 26. In the case of normal and neoplastic colon cancer tissue, 548 differentially transcripts were identified among the 36,125 unique transcripts.
 - 27. All references cited are hereby incorporated by reference herein.
- 28. Sequences tags in Tables 2-4 are consecutively numbered to form SEQ ID NOS: 1-732.

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CLAIMS

1. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of the at least one transcript is found to belower in the first sample than in the second sample.

2. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

- 3. The method of claim 1 wherein a comparison of at least two of said transcripts is performed.
- 4. The method of claim 2 wherein a comparison of at least two of said transcripts is performed.

- 5. The method of claim 1 wherein a comparison of at least five of said transcripts is performed.
- 6. The method of claim 2 wherein a comparison of at least five of said transcripts is performed.
- 7. The method of claim 1 wherein a comparison of at least ten of said transcripts is performed.
 - 8. The method of claim 2 wherein a comparison of at least ten of said transcripts is performed.
 - 9. The method of claim 1 wherein a comparison of at least twenty of said transcripts is performed.
 - 10. The method of claim 2 wherein a comparison of at least twenty of said transcripts is performed.
 - 11. The method of claim 1 wherein a comparison of at least thirty of said transcripts is performed.
- 15 12. The method of claim 2 wherein a comparison of at least thirty of said transcripts is performed.
 - An isolated and purified human nucleic acid molecule which comprises
 SAGE tag selected from SEQ ID NO:1-732.
 - 14. The nucleic acid molecule of claim 13 which is a cDNA molecule.

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- 15. The nucleic acid molecule of claim 13 wherein the SAGE tag is located at the 3' end of the molecule, adjacent to the 3'-most NlaIII restriction enzyme site.
- 16. An isolated nucleotide probe comprising at least 10 nucleotides of a human nucleic acid molecule, wherein the human nucleic acid molecule comprises a SAGE tag selected from SEQ ID NO: 1-732.
 - 17. The probe of claim 16 which comprises the selected SAGE tag.
 - 18. A diagnostic reagent for evaluating neoplasia of a colorectal tissue, comprising at least 2 probes according to claim 16.
- 10 19. The diagnostic reagent of claim 18 which comprises at least 5 probes according to claim 16.
 - 20. The diagnostic reagent of claim 18 which comprises at least 10 probes according to claim 16.
 - 21. The diagnostic reagent of claim 18 which comprises at least 20 probes according to claim 16.
 - 22. The diagnostic reagent of claim 18 which comprises at least 30 probes according to claim 16.
 - 23. A diagnostic reagent for evaluating neoplasia of a colorectal tissue, comprising at least 2 probes according to claim 17.
 - 24. A method of diagnosing pancreatic cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25. A method of diagnosing cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

26. A method to aid in the determination of a prognosis for a colon cancer patient, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of the at least one transcript is found to be lower in the first sample than in the second sample.

27. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

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comparing the level of at least one transcript in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

28. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of expression of the protein is found to be lower in the first sample than in the second sample.

29. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

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30. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

31. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

32. A method of diagnosing pancreatic cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

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33. A method of diagnosing cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

34. A method to aid in the determination of a prognosis for a colon cancer patient, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of expression is found to be lower in the first sample than in the second sample.

35. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

comparing the level of expression of at least one protein in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

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36. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

37. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

38. A method of treating a cancer cell, comprising the step of:

administering to a cancer cell an antibody which specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5, wherein the antibody is linked to a cytotoxic agent.

39. An antibody linked to a cytotoxic agent, wherein the antibody specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5.

40. A method of detecting colon cancer in a patient, comprising the steps of:

comparing the level of at least one protein in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

41. A method of detecting pancreatic cancer in a patient, comprising the steps of:

comparing the level of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

42. A method of detecting cancer in a patient, comprising the steps of:

comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

43. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

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comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

44. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

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comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

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determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

45. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

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comparing the level of expression of at least one protein in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those

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shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

46. A method of detecting colon cancer in a patient, comprising the steps of:

comparing the level of at least one transcript in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

47. A method of detecting pancreatic cancer in a patient, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

48. A method of detecting cancer in a patient, comprising the steps of:

comparing the level of at least one transcript in a first sample to
a second sample, wherein the first sample is of patient and the second sample
is of a normal human, wherein said transcript is identified by a tag selected

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from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

49. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

50. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

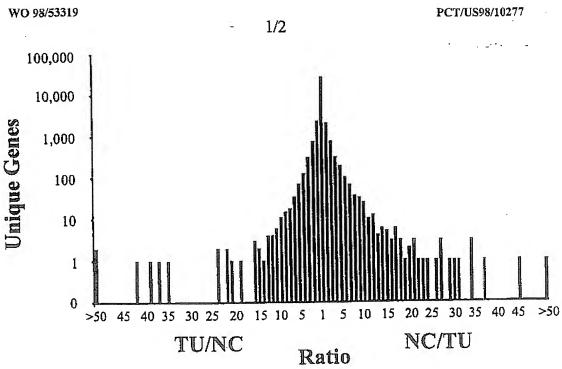
51. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

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comparing the level of expression of at least one transcript in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

52. A method for screening for candidate agents that modulate the expression of a polynuleotide selected from the group consisting of the polynucleotides in SEQ ID NOS:1-732 or their respective complements, comprising contacting a test agent with a colon or pancreatic cell and monitoring expression of the polynucleotide, wherein the test agent which modifies the expression of the polynucleotide is a candidate agent.



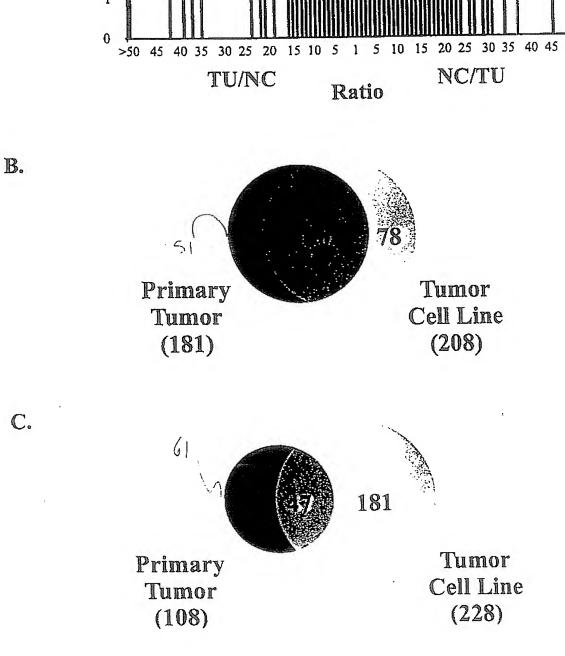


FIG. 2

A.

	1	2	3	SAGE	Data
	TNT	N	N	T	N
			M) 1		
H204104				11	102
H259108				1	37
H1000193			Del.	56	12
H998030	(a) (•	55	7

B.

		Pancreatic Tumors						Normal Colon		SAGE Data		
	1	2	3	4	5	6	7	8	1	2.	Pancreatic Tumors	Normal Colon
					4					H	Lamor	
			<u>. </u>	ا ئىسال				ب		. /		
		224	٠ ^ ٨	inderion in	\$ 0.00 E 0.00	i wiekstu					48	0
H294155						•		幅			47	U
H560056											32	0

C.

	CR Tumors		Pancreatic Tumors			Normal Colon			SAGE Data			
	1	2	3		2	3	1	2	3		Pancreatic Tumors	Normal Colon
H802810					in Belgilland China, and A	eules author **				27	0	1
H85882									\$.	10	26	0
H618841							,	7		8	62	0